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THE UNITED STATES ARMY MEDICAL UNIT

United States Army Medical Research and Development Command

Walter Reed Army Medical Center

Fort Detrick, Maryland

AUTOPSY PROTOCOL

Joel E. Willard

USAMU Accession No. 332

April 1960

AUTOPSY REPORT

Joel E. Willard
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United States Army Medical Unit
Fort Detrick, Maryland

AUTOPSY PROTOCOL: JOEL E. WILLARD

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AUTOPSY PROTOCOL

USAMU Pathology Accession No. 332

Name: WILLARD, Joel Eugene — Nativity: Maryland

Status: D. A. civilian employee, Fort Detrick, Md. — Age: 53 Sex: Male

Admitted: 1100 hours, 30 June 1958 — Race: White

Date and Time of Death: 0105 hours, 5 July 1958

Date and Time of Autopsy: 0300 hours, 5 July 1958

Prosector: Lt. Col. Colin F. Vorder Bruegge, MC

Assistants: Col. W. D. Tigertt, MC
Capt. Richard B. Hornick, MC
Capt. Walter T. Hughes, MC
Doctor Martha K. Ward, USPHS

CLINICAL DIAGNOSES

Direct Cause of Death: Myocardial failure.

Contributory Cause of Death: Visceral Anthrax (012-118).

I. PATHOLOGICAL DIAGNOSES

A. GENERAL

1. MEDIASTINITIS, DIFFUSE; ASSOCIATED CONGESTION AND EDEMA, SEVERE.
2. Ecchymoses and edema; left forearm and arm, right forearm; secondary to needle puncture wounds and intravenous therapy.
3. Needle puncture wound, lower anterior neck, into trachea, surgical.
4. Needle puncture wound, anterior chest, into heart, surgical.
5. Incision, surgical, right arm, with insertion of polyethylene catheter into basilic vein.
6. Arcus senilis, bilateral, slight.
7. Alopecia, partial, frontal and temporal regions, cause undetermined.

B. RESPIRATORY SYSTEM
UPPER

1. Nasal septum deviation to right, cause unknown.
2. Asymmetry of larynx, due to old dislocation of thyroid cartilage and surgical excision of vocal cord nodule one year ago.
3. Laryngitis and tracheitis, acute, with focal mucosal hemorrhage and ulceration.
4. Focal dyskeratosis, right vocal cord.
5. Biopsy of vocal cord, old, healed.

LOWER

1. Hydrothorax, bilateral (right, 700 ml; left, 400 ml).
2. Adhesions of pleurae, between lobes, bilateral, old, fibrous.
3. Pleural and subpleural fibrosis and calcification, old apex of right and left lung; suggestive of healed tuberculosis.
4. Pulmonary congestion, edema and atelectasis, moderate, patchy, bilateral.
5. Bronchitis, acute, bilateral, with mucosal ulceration and peribronchial pneumonitis.
6. PNEUMONITIS, FOCAL, NODULAR, WITH HEMORRHAGE AND NECROSIS, RIGHT MIDDLE LOBE.

C. LYMPHATIC AND HEMATOPOIETIC SYSTEMS

1. Splenitis, acute.
2. Accessory spleens (two).
3. Cyst of spleen, subcapsular.
4. Lymphangitis, acute and chronic; lymphatics of lungs, mediastinum and neck.
5. LYMPHADENITIS, ACUTE, SEVERE, WITH EXTENSIVE HEMORRHAGE AND NECROSIS; TRACHEOBRONCHIAL, MEDIASTINAL AND CERVICAL NODES. (BACILLUS ANTHRACIS IDENTIFIED BY CULTURE, FLUORESCENT-LABELLED ANTIBODY STAINS, AND BROWN AND BRENN STAINS IN NODES AT TRACHEAL BIFURCATION AND AT LOWER POLE OF THYROID.)
6. Lymphadenitis, acute, nodes other than No. 5.
7. Focal calcification and fibrosis, right tracheobronchial nodes.
8. Bone marrow hyperplasia, minimal.
9. Fatty atrophy of thymus.

D. CARDIOVASCULAR SYSTEM

1. Arteriosclerosis, generalized, moderate, including pulmonary arteries.
2. Vascular stasis, generalized, severe; cyanosis of head and neck.
3. Pericarditis and epicarditis, minimal.
4. Myocardial edema, moderate.
5. Thrombi, old, small arteries and veins of lung, prostate gland and spermatic cord.
6. Thrombi, recent, small veins of multiple organs, principally in thorax and neck.

E. GASTROINTESTINAL SYSTEM

1. Absence (extraction) of upper right premolar tooth (R-5).
2. Pharyngitis, acute.
3. Esophagitis, acute, with mucosal ulceration and hemorrhage.
4. Enteritis, acute (jejunum), focal, with mucosal ulceration.
5. Fibrous obliteration, appendix, distal third.
6. Passive congestion, liver, moderate.
7. Cholecystitis, chronic, minimal, with cholelithiasis.

F. GENITOURINARY SYSTEM

1. Solitary cyst, right kidney; multiple small cortical cysts, bilateral.
2. Pyelonephritis, minimal, bilateral.
3. Arteriolar nephrosclerosis, minimal.
4. Cystitis, acute, minimal, with focal hemorrhages at trigone.
5. Degeneration and atrophy of testes, slight.
6. Cysts and calculi, epididymis.
7. Cysts of seminal vesicles, small.
8. Prostatitis, chronic, minimal.

G. ENDOCRINE SYSTEM

1. Lipid depletion, adrenals, moderate.

H. CENTRAL NERVOUS SYSTEM

1. Vascular stasis, diffuse, severe, with multiple perivascular hemorrhages.
2. Anoxic encephalopathy, moderate.
3. Calcification, advanced, pineal.
4. Leptomeningitis, minimal.

II. CLINICAL ABSTRACT

Ward 200, WRAH
Register No. 4929059

WILLARD, Joel E.
USAMU Pathology Accession No. 332
5 July 1958

A. PRESENT ILLNESS

This 53 year old, white, male electrician was admitted to the hospital at 11:00 a.m. on June 30, 1958, because of fever, severe frontal and occipital headache, and generalized muscular aches which had begun abruptly the previous day at 1:00 p.m. Aspirin produced no relief. He had been seen briefly in the Outpatient Service prior to admission where he was considered to have a possible infection with the virus of Venezuelan equine encephalomyelitis.

B. FAMILY HISTORY

His father died at the age of 84, cause unknown. His mother died at the age of 68 presumably of pneumonia. Six siblings are living and well. His wife and an adult son are living and well. There is no history of familial diseases.

C. PAST HISTORY

1. Medical

He had been a healthy vigorous worker. Interviews with associates and review of work performance records indicated exceptionally rare absences from duty because of illness during the past thirty years. Records of his family physician disclosed no previous serious illnesses or injuries. He had never been in the Armed Forces. Fort Detrick records indicate no absence from work due to sickness for several years prior to 1957; in that year he had required treatment for a lesion of the larynx. He did not recall any serious illnesses or injuries during childhood. No significant abnormalities were found at annual physical examinations from 1930 to 1937 while he was employed as a bus operator, nor from 1938 through 1951 when he worked part-time as a fireman. Associates stated that he visited the Mobile X-ray Unit of the Frederick County Tuberculosis Association for routine annual chest x-ray examinations from 1948 through 1951. The Association has no record of recognized abnormalities (films considered "negative" are discarded after one year).

In December, 1952, no significant abnormalities were detected on pre-employment chest x-ray and physical examination at Fort Detrick. He stated specifically that he had no known physical defects or disability. At that time urinalysis and a serological test for syphilis were negative. Outpatient records disclose no evidence of serious illness or injury prior to his terminal disease.

In May, 1955, he visited his family physician because of "pain in sides, back pain, indigestion and bloating." Physical examination disclosed no abnormality except carious teeth. A trace of sugar was found in the urine. Following symptomatic treatment recovery was apparently prompt and complete.

In March, 1957, he was seen by the family physician because of persistent and increasing hoarseness during the previous month; no definitive diagnosis was made. Urinalysis revealed a trace of sugar. His hoarseness became worse during the next six weeks. Chest x-ray examination at Fort Detrick on May 13 did not show significant changes. His physician referred him to a specialist at Eye, Ear, Nose and Throat Hospital, Hagerstown, Maryland, where he was first seen May 17, 1957. He had no history of symptoms characteristic of any allergic manifestations. It was not possible to visualize the larynx completely during this office examination, but a lesion was thought to exist somewhere in the region of the anterior commissure. He returned May 24 for direct laryngoscopic examination and was admitted to Washington County Hospital, Hagerstown. A small hyperkeratotic nodule was found on the anterior commissure of the right vocal cord. Biopsy disclosed a hyperkeratotic lesion with evidence of early carcinomatous change. The surgeon was confident the lesion was not extensive and thought it was probably a carcinoma-in-situ. However, he was not able to visualize the larynx completely even during direct laryngoscopy. He thought this was due to lack of adequate muscle relaxation not fixation due to invasion by carcinoma and in part to marked enlargement of the epiglottis, considered congenital. Two weeks later the patient returned to have laryngoscopy repeated while under general anesthesia. An excisional biopsy showed an intraepithelial carcinoma still present in the right vocal cord. A third biopsy on July 22 from the site of the excised neoplasm showed normal tissues with no evidence of remaining carcinoma. Follow-up examination on August 30 disclosed normal healing and no tumor recurrence. No x-ray examinations were made by hospitals in Hagerstown.

His last visit to the family physician was on March 15, 1958, because of complaints of "bloating, abdominal pain, yellow stools, gas and burping." He was successfully treated with Probanthine. His physician has no record of any x-ray examinations.

On May 1, 1958, at Fort Detrick, physical examination, chest x-ray and an electrocardiogram disclosed no significant abnormalities. A serological test for syphilis and urinalysis were negative.

Since employment in 1952 he had been immunized for a number of infectious agents under study at Fort Detrick, but not against anthrax. Procedures performed during the period immediately preceding his terminal illness were:

June 16, 1958 - Yellow fever vaccination (Strain 17D, 0.5 ml).
- Tularemia skin test (Foshay) - negative.
- Brucellosis skin test (Brucellergen) - negative.

June 18, 1958 - Tularemia vaccination (Foshay, 0.25 ml).

June 19, 1958 - Tularemia vaccination (Foshay, 0.5 ml).
- Smallpox vaccination. (Immune reaction. Previous reactions: May 13, 1953, none; May 20, 1953, primary; March 8, 1955, immune.)

Two weeks prior to admission a right upper premolar tooth had been extracted; healing was normal. No complications were recognized.

2. Habits

He stopped smoking in May or June, 1958. Prior to this time he had been a moderate pipe smoker. He did not drink alcoholic beverages of any kind. Investigation of dietary habits revealed no unusual characteristics. He enjoyed a wide variety of food, and frequently ate fresh meat and vegetables.

3. Occupational

He was born December 21, 1904, and had lived in the vicinity of Frederick, Maryland, and Washington, D. C., all his life.

For a short period prior to 1921 he drove a truck for the M. J. Grove Lime Co., Frederick, Maryland. Exact duration of employment is not known. Contact with lime, cement, gravel and other building materials was limited mainly to loading and unloading a truck, although he occasionally worked in a warehouse.

From 1921 through 1951 he worked as an electrician for Hahn Electric Co., with the exception of the period 1930 to 1937 when he was employed as a bus operator in Washington. From 1938 to 1951 he and a fellow worker alternated days working as electrician and fireman for the Independent Hose Co., Frederick. At the fire company his principal duties were to drive the engine and serve as caretaker for company property; he occasionally acted as firefighter. He was never overcome by smoke. Most of his time as an electrician was spent in installing wiring and electrical equipment in residential, commercial and school buildings. More than half his work was in new school buildings and he was closely associated with men using different building materials, including a variety of products for insulation of attics and walls. He frequently installed or repaired lighting fixtures and often handled fluorescent light tubes. During much of this period the phosphor powders contained beryllium (4 to 12 per cent beryllium, expressed as the oxide), but associates state that he was rarely assigned to destroy or dispose of discarded tubes, and there is no history of injury by broken tubes.

For approximately six years he had been employed at Fort Detrick as an electrician; in the course of his job he regularly entered laboratory buildings in which a variety of pathogenic organisms were under study. Work assignments included the wide range of duties associated with installation and maintenance of electrical circuits and equipment in modern laboratories.

He took his turn with other Electrical Shop workers at grinding discarded fluorescent light tubes. The bulbs, prior to burial in a remote area, were pulverized under water in the open by a device developed at Fort Detrick in 1948 to prevent workers from breathing the phosphor dust released at the time of breaking glass. There is no evidence he was exposed more intimately than other workers to broken fluorescent tubes; others on the staff have had no illnesses or findings on medical examination to indicate harmful effects from this procedure.

During the two weeks prior to terminal illness he had worked in ten different buildings, in eight of which experimental studies with infectious agents were being conducted. He had performed such tasks as changing electrical cords on contaminated ovens, removing false ceilings to work on vent lines, cleaning motors, examining electrical panels and circuits, installing U.V. lights in animal rooms, changing light bulbs, and changing or repairing fixtures in hoods. There had been no known breaks in technique in any of these buildings, nor had illness in other personnel been observed. Extensive culturing of material from various surfaces and equipment in these buildings after his illness disclosed Bacillus anthracis in very small numbers from three buildings and the patient's tool pouch.

During recent years he had led an urban life; he lived within the city of Frederick and had no intimate contact with farm environment.

(Dr. Paul J. Kadull, Chief, Medical Investigation Division, Fort Detrick, furnished from his files and personal correspondence much of the data on the patient's past history.)

D. ADMISSION PHYSICAL EXAMINATION

This well nourished male did not appear acutely ill. Rectal temperature was 103.6°F, pulse, 80 per minute, respiration, 20 per minute, and blood pressure 128/78 mm Hg. He was clear mentally; no neurological abnormalities were detected. No peripheral lymphadenopathy was noted. There was partial obstruction of both nasal passages, more marked on the right. His throat was mildly hyperemic and there was a postnasal exudate. Phonation was normal. The site of recent tooth extraction was well healed. There were no masses in the neck, no edema and no discoloration. His chest was symmetrical with good respiratory movements. Lungs were clear to percussion and auscultation. Heart sounds were normal. No masses were felt in the abdomen. A rectal examination was negative with the exception of a small firm mass palpated in the right lobe of the prostate gland.

E. ADMISSION LABORATORY AND X-RAY EXAMINATIONS

His admission leukocyte count was 8,100 with 56 per cent segmented and 28 per cent band forms, hemoglobin was 16 gm per cent, hematocrit, 47 per cent, sedimentation rate, 17 mm per hour, and C-reactive protein, 2+. Urinalysis showed a specific gravity of 1.020, negative albumin and a trace of sugar. A chest film showed symmetrical widening of the upper mediastinum, apical capping, and a focal area of consolidation in the right mid-lung field (Figure 1). Films of the pelvis and skull showed normal architecture. The usual routine of collecting pharyngeal washings and blood for culture was followed.

F. HOSPITAL COURSE

He spent a fairly comfortable day and night; the maximum rectal temperature of 104.8°F was reached at 8:00 p.m. after which it slowly dropped during the next 24 hours to 103.6°F.

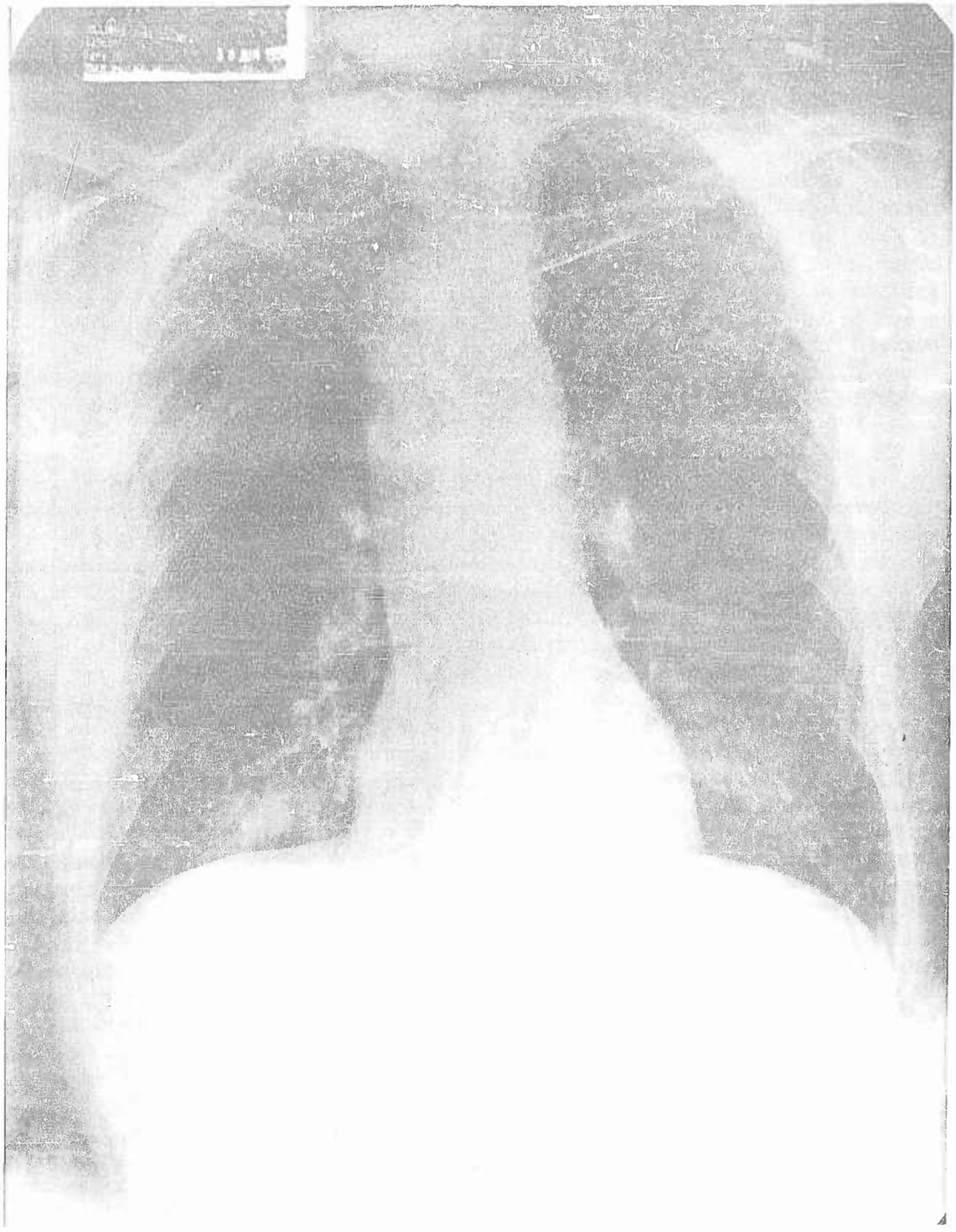

FIGURE 1. ADMISSION CHEST X-RAY DAY 2 OF DISEASE.

In the morning of the day after admission (July 1) his headache had almost disappeared. The leukocyte count was 14,950 with 44 per cent segmented and 38 per cent band forms, hemoglobin, 17 gm per cent and the C-reactive protein test, 4+. A test for cold agglutinins was negative. Postprandial blood sugar at two hours was 158 mg per cent. The acid and alkaline phosphatase values were within normal limits. Morning chest films on this date showed no change other than focal linear atelectasis in the left lower lobe. There were no significant physical findings on examination of the chest. In the late afternoon, a 24-hour reading of the blood cultures was reported negative. Additional roentgen films taken at this time showed some obscuring of the left costophrenic angle; presence of fluid was also observed in a lateral projection. Because of these signs of progressive intrathoracic involvement and despite a drop in temperature, broad spectrum antibiotic therapy was begun. Because of nausea and vomiting, and possible dehydration, tetracycline (Achromycin: initial dose one gram per 12 hours) was given in 1,000 ml of intravenous glucose starting at 9:00 p.m., 33 hours after admission and 54 hours after onset of illness. The working diagnosis at this time was mediastinitis, probably due to B. anthracis; this impression was reached by exclusion, possibility of exposure during his work, and appearance of the small amount of pleural fluid.

During the night he developed a slight hacking cough and early the following morning (July 2), with much persuasion, produced a small amount of sputum which on direct smear contained a few Gram positive rods. Examination of blood cultures of June 30 and July 1 now showed scattered discrete colonies resembling B. anthracis. During the course of the day identification was confirmed by bacteriophage lysis and by the characteristic colonial morphology on penicillin agar, i.e. "string-of-pearls". Antibiotic sensitivity studies showed the organisms to be sensitive to penicillin, chloromycetin, the tetracyclines, streptomycin, furadantin, erythromycin, and neomycin. Cultures of sputum and vomitus did not yield B. anthracis although on direct smear the specimens contained Gram positive rods. After death, the pharyngeal washings and sputum inoculated into guinea pigs were negative for B. anthracis.

Throughout the day of July 2, except for slight dehydration and nausea, the patient appeared well and felt better. Rectal temperature ranged between 101.6° and 103.8°F; the pulse remained at 80 to 100, and the blood pressure was 110/70. Morning laboratory work showed a leukocyte count of 12,350 with 42 per cent segmented and 40 per cent band forms; hemoglobin was 18.5 gm per cent and hematocrit, 57 per cent. Blood urea nitrogen was 25 mg per cent and serum chloride (as NaCl) was 99.5 mEq/L. Urine specific gravity ranged between 1.035 and 1.040 with only a trace of protein. During this 24-hour period, he received 3,195 ml of fluid, primarily by the intravenous route; output was 1,305 ml (1040 ml urine and 265 ml vomitus).

Bedside roentgen films showed haziness in both bases and an apparent slight increase in pleural fluid bilaterally. Tetracycline was continued intravenously at a rate of one gram every 12 hours; a chemical phlebitis developed. An electrocardiogram showed no abnormality (single segments of all tracings are shown in Figure 2).

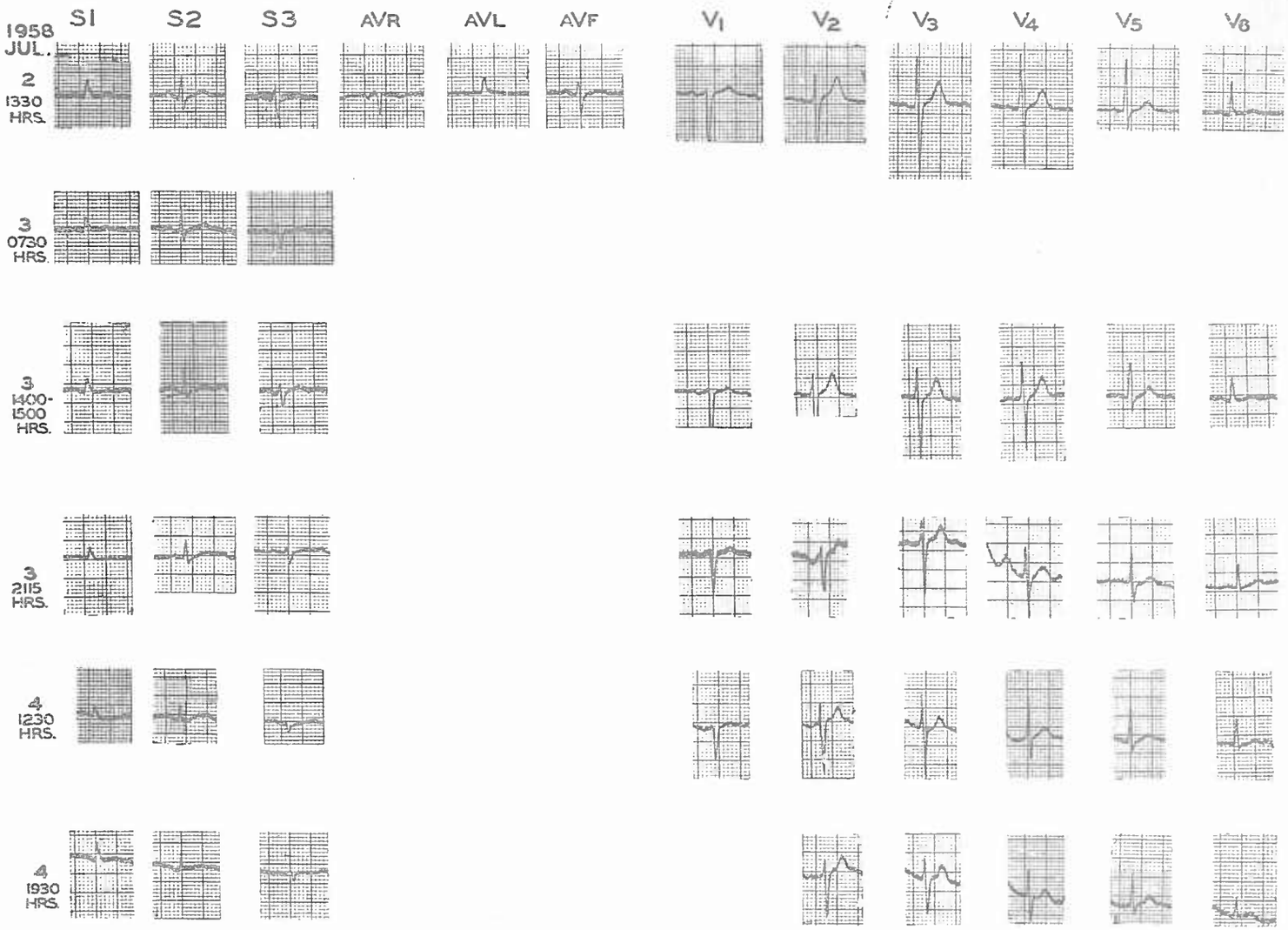

FIGURE 2. SERIAL ELECTROCARDIOGRAMS OF DAYS 4 THROUGH 6 OF DISEASE.

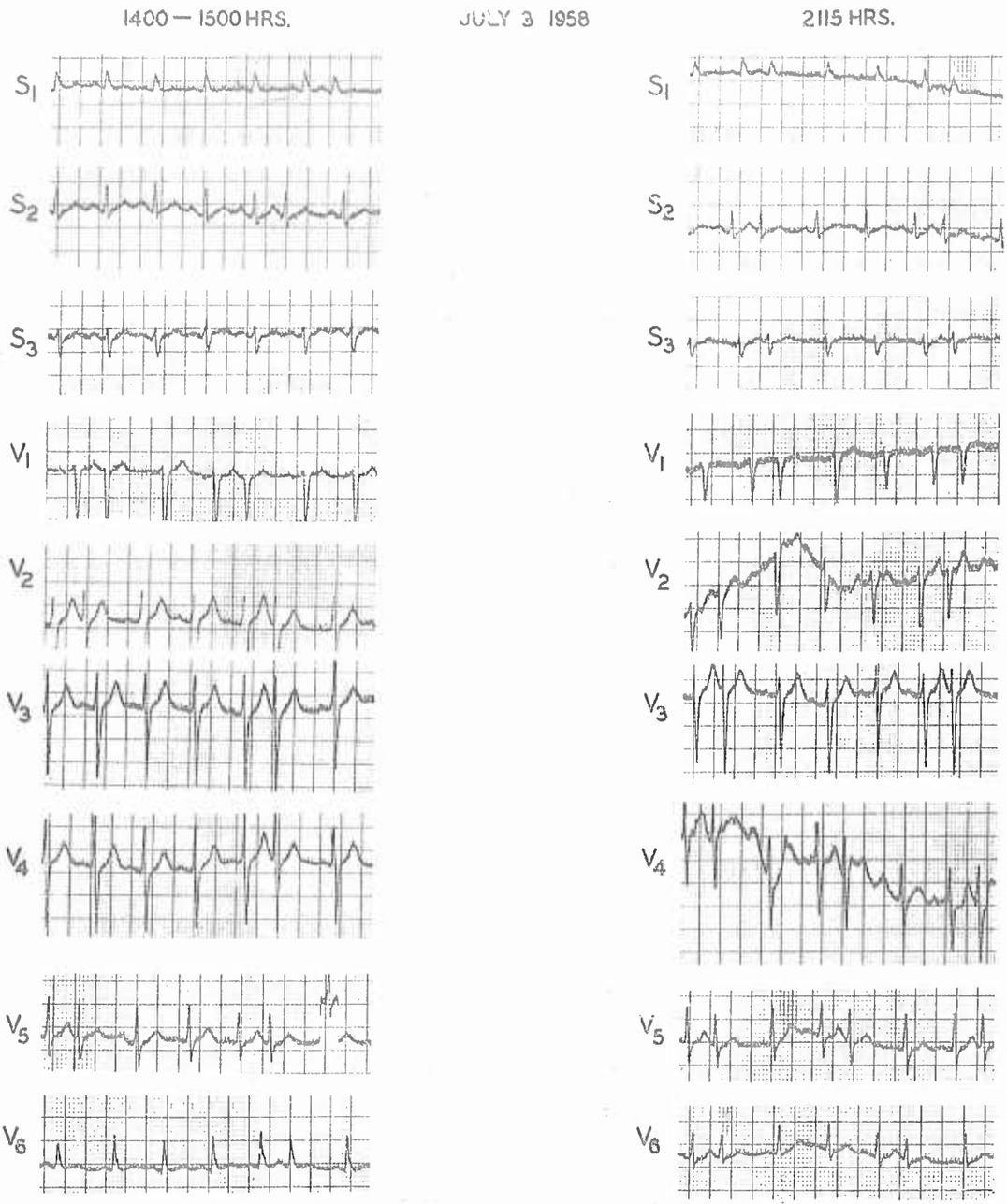

FIGURE 3. ELECTROCARDIOGRAMS OF DAY 5 OF DISEASE SHOWING BIGEMINY.

On the morning of July 3 the patient was alert; rectal temperature was 101.8°F, blood pressure, 110/80, and pulse, 110 per minute, in contrast to previous relative bradycardia. A morning electrocardiogram showed no change except for an increased rate. Scattered coarse rhonchi were present, which readily cleared on deep breathing. Chest x-ray examination with a portable bedside unit showed no change in mediastinal configuration and an increase in pleural fluid bilaterally. The leukocyte count was 11,850 with 34 per cent segmented and 38 per cent band forms.

Examination at noon on July 3 revealed a pulse rate of 120 and physical signs suggestive of pulsus alternans. Afternoon and evening electrocardiograms showed bigeminy (Figure 3). The pulse rate continued to increase, reaching 140 per minute, during the evening. Associated with this gradual increase in pulse rate were tachypnea, apprehension and clouding of the sensorium. Administration of oxygen by nasal catheter was begun and small doses of demerol were given. By midnight the cardiac irregularity had disappeared, although the pulse remained rapid.

Total fluid intake for July 3 was 3,600 ml and urine output was 1,760 ml. Urine specific gravity ranged around 1.032; a trace of protein was detected on several determinations. The tetracycline blood level, determined on a specimen obtained some 36 hours after initiation of therapy was 11 µg/ml; the drug was also present in large quantity in the urine.

On July 4 when the nasal catheter was removed, cyanosis was noted; oxygen was then continued by tent. Expiratory wheezes were evident in the right lung, none in the left lung. Rectal temperature was 101.8°F, pulse, 110 per minute and regular, and blood pressure, 135/85. The urine had a specific gravity of 1.024 and a trace of protein. The leukocyte count was 15,000 with 27 per cent segmented and 39 per cent band forms. The hematocrit was 50 per cent.

During the course of the day the patient was lucid and not cyanotic. Urine output continued satisfactorily and there was no peripheral edema. The pulse rate increased but remained regular. Blood pressure was maintained within normal limits. Roentgen films were of poor quality but showed focal areas of density throughout the lung fields with bilateral pleural fluid; no change was evident in the mediastinal area. He became more restless and apprehensive during the afternoon and breathing became labored. Attempts to remove material from the respiratory tract by suction were only partly successful; a small amount of bloody, tenacious bronchial secretions were obtained. At midnight respirations were at the rate of 36 per minute and labored. At 1:05 a.m., July 5, he suddenly became agitated and respiration ceased.

Laboratory examinations are summarized in Figure 4, clinical findings, in Figure 5.

WILLARD, JOEL E. USAMU PATH. ACC. NO. 332, 5 JUL 58	DATE: 1958	29 JUNE	30	1 JULY	2	3	4	5
	DAY OF DISEASE	1	2	3	4	5	6	7
URINALYSIS								
SPECIFIC GRAVITY			1.020		1.040	1.032		
ALBUMIN			–		+	TR.		
SUGAR			TR.		3+	3+		
RBC			+		+	–		
WBC			+		+	+		
CASTS			–		+	+		
BLOOD CHEMISTRY								
POTASSIUM	MEQ/L				4.2			
SODIUM	MEQ/L				136			
CHLORIDES (AS NaCl)	MEQ/L				99.5			
CO_2	VOL %				52			
UREA NITROGEN	MG %				25			
GLUCOSE (2 HR PP)	MG %			158				
ACID PHOSPHATASE	U.			0.22				
ALK. PHOSPHATASE	U.			1.6				
CSR	MM/HR		17	7	3	3	1	
HEMATOCRIT	%		47	51	57	51.5	50	
HEMOGLOBIN	GM %		16.1	17.0	18.5	17.0	17.0	
CRP			2+	4+	4+	4+	4+	
WBC NO./CMM (MONO., LYMPH., BAND, NEUT.; 15,000 / 10,000 / 5,000)								
B. ANTHRACIS ISOLATION CULTURE/ANIMAL INOCULATION: BLOOD			—	—		—		
GASTRIC WASHING					—			
PHARYNGEAL WASHING			—	—	—			
VOMITUS					— *			
SPUTUM					— —*			
VDRL						NEG.		
HOSPITAL DAY			1	2	3	4	5	6

* GRAM POSITIVE ROD ON DIRECT SMEAR

FIGURE 4. SUMMARY OF LABORATORY EXAMINATIONS.

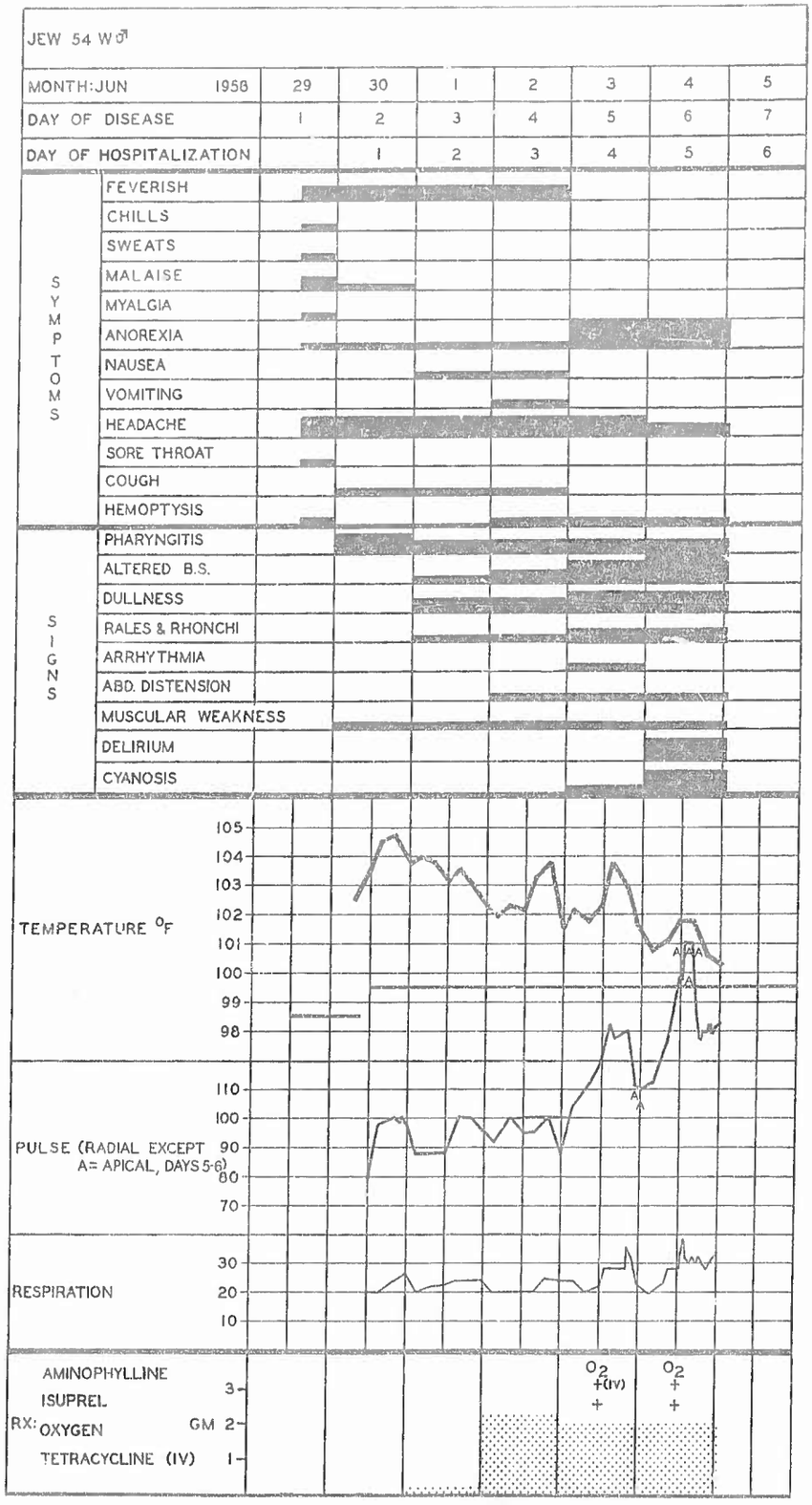

FIGURE 5. CLINICAL SUMMARY.

G. COMMENT

There are several significant features in this case, the most outstanding being the picture presented on admission to the hospital: although the patient was uncomfortable and febrile, he in no way appeared seriously ill on admission; roentgen evidence of widening of the upper mediastinum was evident and did not materially change during the course of the disease. As is true of all patients admitted, anthrax was considered in the differential diagnosis. Probability of this infection was discounted because of the remarkable disparity between the marked enlargement of the mediastinum and the generally benign clinical picture. The change in the leukocyte picture and the appearance of pleural fluid on repeat roentgen examination caused reconsideration and initiation of therapy, despite the subjective improvement, the gradual drop in temperature, and a negative blood culture. Confirmatory evidence was obtained 12 hours later by blood culture findings.

The source of this infection has not been determined, although it must have been by inhalation; the organisms probably passed to paratracheal and mediastinal lymph nodes, resulting in mediastinitis, obvious at 24 hours after the initial fever. Since the evidence of mediastinitis did not change on subsequent examination it seems permissable to speculate that discernible roentgen change may have been present much earlier, perhaps at the time of the onset of fever.

After its onset the temperature gradually dropped over succeeding days, and showed a diurnal swing of about two degrees. At no time was there evidence of renal impairment; blood pressure remained within normal limits despite the episode of cardiac irregularity and subsequent tachycardia.

At the time of his death preparations were being made for a tracheotomy, to permit direct aspiration of bronchial secretions in the belief that their presence was a major cause of his respiratory difficulties.

The duration of clinical illness was five and one-half days, the patient having been on continuous intravenous tetracycline since the 54th hour of his disease.

III. GROSS EXAMINATION

A. GENERAL

The body of this well-developed, well-nourished, 54 year old, white male weighs 165 pounds and measures 5' 10" in length. There is slight livor mortis, no rigor mortis, and the body still maintains some natural warmth. Peripheral lymphadenopathy cannot be demonstrated. Skin texture and subcutaneous tissue turgor are normal except for upper extremity changes secondary to needle puncture wounds and intravenous therapy. Lower extremities are bilaterally symmetrical, muscular, and appear normal except for slightly increased prominence of the superficial veins. The left forearm and lower third of the upper arm are moderately edematous; edema of the right forearm is barely detectable. Both hands are normal. A mottled, dark reddish-purple, ecchymotic area extends up the radial aspect of the left forearm along the cephalic vein from a point immediately above the wrist to the antecubital fossa. Numerous needle puncture wounds lie along the courses of all major superficial veins in both forearms. Tissues about these vessels are indurated; overlying skin is reddened. A polyethylene catheter enters the right basilic vein 11 cm above the elbow thru a linear surgical incision measuring 3.5 cm; it is closed with interrupted black silk sutures; the incision is recent, clean, easily opened, and lies at right angles to the long axis of the vein.

Cyanosis is marked over the entire head and neck; dark greyish-purple discoloration is most pronounced in the ears, lips and scalp. Cyanotic regions at the base of the neck are clearly demarcated from more normal skin areas of the chest and shoulders. Skull contour is normal. Growth of greying dark brown hair is normal over posterior and lateral scalp areas; hair is sparse or absent over frontal regions. Superficial scalp veins are strikingly dilated and tortuous. Ears, external auditory passages and lips are not remarkable except for cyanosis. Nasal mucous membranes are diffusely congested; focal lesions are not seen. Right nasal passages are almost occluded by septal deviation and an accumulation of a small amount of grey-yellow mucoid material. The left nasal passage is open. Small amounts of mucus lie in patches on the moist mucosa. Both eyes are directed forward. Pressure in the globes of both eyes is normal. Conjunctivae are moist, uniform and clear; dilated superficial capillaries are tortuous and unusually prominent. There is barely detectable arcus senilis. The pupils are equal, central, round and regular and measure 5.0 mm in diameter. Eyebrows are normal. Lacrimal glands are not dissected; no abnormalities are detected on palpation. Orifices of lacrimal ducts appear normal.

A 2- to 3-day growth of greying beard is distributed normally over the face. A small mustache is neatly clipped. The neck is well-developed, firm, symmetrical and without abnormal masses. A recent needle puncture wound is located directly over the trachea in the suprasternal notch, 5.0 cm above the manubrium. Subcutaneous tissues of the anterior neck are crepitant. The thorax is symmetrical; musculature is firm and well-developed. Grey hair grows sparsely over the upper anterior chest; hair has been shaved recently from the midanterior chest. Abnormalities are not seen in the nipples. A heavy growth of dark brown hairs measuring 0.5 to 2.0 cm is present about each

nipple in irregularly circular areas measuring 8.0 to 10.0 cm in diameter. A recent needle puncture wound is present in the fith left intercostal space, 2 cm from the midline. The abdomen is slightly protuberant, firm and doughy. Abnormal masses are not felt. No operative scars are seen. The umbilicus is clean and normally formed. Inspection of external genitalia discloses no abnormalities. Both inguinal rings are slightly larger and more relaxed than normal but there is no hernia. The anus is not remarkable. No significant abnormalities are detected over the back or buttocks; subcutaneous fat is firm and normal in distribution and amount.

B. PRIMARY INCISION

The body is opened by a conventional Y-shaped incision from each axilla to the midanterior chest, then directly down the midline to the symphysis pubis. No abnormalities are seen in the skin or the firm, bright yellow, subcutaneous fatty tissues. Thickness of the fatty layer is 3.0 cm at a point 3.5 cm superior to the umbilicus and 1.5 cm over the sternum at the level of the nipples. Thoracic musculature is dark red-brown, well-developed and of normal texture. Non-clotted, reddish-black blood oozes from severed blood vessels in all regions of the thoracic wall and mediastinum. There is little or no calcification of the costal cartilages; all cut easily with a sharp knife. Both pleural cavities contain clear, light-yellow fluid; approximate amounts are 700 ml in the right cavity and 400 ml in the left cavity. Adhesions between parietal and visceral pleurae are not found, and parietal pleurae are smooth, grey-white and of uniform thickness. The diaphragm has normally formed lumbocostal arches, crura and central tendon; attachments to the xiphoid process, ribs and lumbar vertebrae are at normal levels; openings for the aorta, esophagus, vena cava and smaller structures are not remarkable. The maximum height of the right dome is to the level of the lower margin of the fifth rib at the costochondral junction; the left dome reaches to the upper margin of the sixth rib at the costochondral junction. The pericardial sac contains approximately 5.0 ml of slightly cloudy, faintly pink, serous fluid; there are no adhesions, and the lining surfaces are smooth, glistening and grey-white. Pericardial extensions about the roots of the great vessels and reflections to pleural surfaces are normal. Abdominal viscera lie in normal positions. No adhesions or excess fluid are found. Peritoneal surfaces are smooth and glistening. The stomach and intestines are moderately distended with gas. The visceral peritoneal fold and ligaments are not remarkable. The greater omentum is free from adhesions and normally formed, and contains the usual amount of firm yellow fat. The epiploic foramen displays no unusual features. Arrangement of the pelvic structures is normal.

Superior and posterior parts of the mediastinum are two to three times normal width. This widening is due principally to tremendous lymph node enlargement, diffuse edema, congestion of mediastinal soft tissues, and dilation of the venae cavae, their major tributary veins and the pulmonary vessels. These abnormalities are present at the superior aperture of the thorax and involve comparable structures in the neck. Lymph nodes are involved in all parts of the mediastinum but the lower right paratracheal and anterior bronchial nodes are the most markedly enlarged. Supporting soft tissues are watery, translucent and grey-pink or grey-red; serosanguinous fluid drips from cut surfaces. Soft tissues are firmer, darker red and, in some regions, frankly hemorrhagic when compared to severely involved lymph

nodes immediately adjacent. Soft tissue edema and stasis are comparable in all parts of mediastinum; superior and posterior parts display more widening than the anterior and middle parts because of greater lymph node population. A most striking finding is the relocation of the right mediastinal wall. Spaces between nodular masses of nodes and dilated veins have been so completely and regularly occupied by swollen soft tissues that the parietal pleura forms a remarkably smooth and regular sheet lying in an almost straight vertical line as viewed anteroposteriorly.

C. RESPIRATORY SYSTEM

1. Asymmetry of nasal passages has been noted. Portions of the nasal conchae observed thru the nares are not unusual except for mucosal congestion. The frontal, ethmoidal, sphenoidal and maxillary sinuses are not opened.

2. Larynx: The epiglottis is covered by intact smooth mucosa; it is slightly larger than normal. Its anterior surface is uniformly grey-pink. Scattered over the posterior surface are numerous, dark red-brown, focal areas measuring 1.0 to 7.0 mm. These sites are not elevated, have poorly demarcated margins, and appear to be regions of extreme stasis or focal hemorrhage. Consistency and elasticity of the epiglottid cartilage are normal. It is slightly asymmetrical. In the greatest transverse dimension it measures 2.5 cm from the midline to the left lateral margin; the corresponding measurement on the right is 2.0 cm. Margins are normally smooth, rounded and regular. Thyro-epiglottic and hyo-epiglottic ligaments display no unusual features nor does the hyoid bone.

The thyroid cartilage is asymmetrical. Its two laminae meet and fuse normally in the midline at their lower margins, but in the superior thyroid notch the upper border of the left lamina lies 6.0 mm posterior to the corresponding region of the right lamina, causing the laryngeal prominence to be formed exclusively by the right lamina. In this region, the two cartilages are joined by tough, grey-white, non-cartilaginous tissue. The superior border of the left lamina is displaced approximately 6.0 mm posteromedially; the superior border of the right lamina is displaced slightly less in an anterolateral direction. No significant abnormalities are noted in the cricoid cartilage, nor in the various ligaments and muscles attaching to it and to the thyroid cartilage. Principal nerves and arteries lie in normal positions. External measurement of the greatest transverse diameter at the level of the upper border of the thyroid cartilage is 6.0 cm; measurement between the superior cornua of the thyroid cartilage is 5.5 cm; the length of the larynx along its anterior wall is 4.5 cm; the greatest anteroposterior diameter, measured externally, is 4.4 cm at the level of the laryngeal prominence.

That portion of the laryngeal cavity below the vocal cord level has normal conformation and volume. Space in the vestibule appears normal but the cavity is asymmetrical, due to displacement of thyroid cartilage laminae and to minimal scarring and contraction of the right vocal cord area, presumably a result of previous surgery in this region. These changes cause the vestibular cavity to lie more to the left than right of midline. No abnormalities are found in the arytenoid, cuneiform or corniculate cartilages, nor in their ligaments.

Ventricular folds and vocal cords are covered by intact mucosa and are normally formed, except for previously mentioned slight irregularity and thickening of the right vocal cord. This area is not well demarcated; it involves the anterior half of the right vocal fold. In this region the fold is thicker and firmer than normal, and the overlying mucosa is slightly roughened and wrinkled. The laryngeal mucosa is diffusely congested and appears slightly edematous. A few, scattered, irregular, dark red-brown foci measuring 1.0 to 3.0 mm contrast sharply with the surrounding grey-red background; these foci are most numerous near the posterior attachments of ventricular and vocal folds and the region immediately above the origin of the trachea. The appearance suggests focal or submucosal hemorrhages or extreme stasis.

3. Trachea: The position, course and conformation of the trachea are normal. It is patent throughout and has an average side-to-side diameter of 2.3 cm. The mucosal lining is mottled dark grey-red with scattered foci of stasis or hemorrhage similar to those noted in the larynx. No definite mucosal ulcerations are detected, but in several regions the surface is more granular and rough than usual, suggesting epithelial erosion. Congestion and epithelial changes are more marked in the lower third. Thin layers of thick, grey, translucent, mucoid material adhere to the mucosa in several areas; no large accumulations of mucus or other material are present. Main stem and subsidiary bronchi arise normally, follow normal courses, and have usual structure. None is occluded although several smaller bronchi contain small accumulations of soft, semi-solid, grey, translucent mucus that partially fill the lumina. All have dark grey-red, intact but somewhat granular, mucosal lining surfaces. It is interesting to note that lumina of the trachea and bronchi are nowhere significantly narrowed by the tremendously enlarged hemorrhagic lymph nodes almost completely surrounding them in many regions.

4. Lungs: Thoracic contents are removed as a single block specimen; the weights of the lungs are not determined. The right lung is covered by intact pleura with no adhesions to the parietal pleura. String-like, tough, grey-white adhesions at several points bridge the interlobar fissure separating the right upper and middle lobes from the lower lobe. The interlobar fissure between the right middle and upper lobes is almost completely obliterated by membranous, thin, grey, tough, translucent adhesions; strong and dense adhesions also bind opposing pleural surfaces of these lobes. Pleura over the right apex is thickened, wrinkled and rubbery in a fairly well delineated cap-like area of approximately 3.0 x 4.0 cm. Multiple sections disclose an irregular superficial zone of firm, grey-white tissue with foci of calcification and a maximum thickness of 0.5 cm. The midinferior surface of the middle lobe is slightly roughened and granular in a poorly demarcated, firm, slightly elevated and rounded, dark red-purple area measuring approximately 5.0 x 6.0 cm. Adjacent regions and opposing surfaces of the lower lobe display patchy and confluent, dark grey-purple areas with an appearance suggesting subpleural hemorrhage or extreme stasis. Sections through the firm area of the middle lobe disclose a subpleural, sharply demarcated, oval, 2.0 x 1.5 x 1.0 cm, dark red-brown lesion 1.5 cm posterior to the middle of the inferior lobe margin anteriorly (Figure 6). Much of its central area is composed of friable, red-black material with an appearance suggesting a blood clot. This focal lesion is surrounded by a non-crepitant, rubbery, dark grey-purple zone with rather clearly delineated margins; more

Figure 6. Lung, right middle lobe, cut surface. Focal, nodular, hemorrhagic lesion surrounded by relatively normal parenchyma. (Tissues fixed in 10% formalin for several days before photographing.)

peripherally the lung parenchyma is crepitant and relatively normal (Figure 6). Except for the lesions at the apex and in the middle lobe, peripheral portions of all lobes are covered by smooth glistening pleura and are of only moderately diminished crepitancy. Pleural surfaces display a mosaic pattern, with irregularly anastomosing linear deposits of anthracotic pigment contrasting with the mottled grey or grey-red background. All lobes are less crepitant and more congested near the hilum than peripherally. Congestion and edema in this lung are most marked in the lower posteromedial portions of the lower lobe.

The left lung is covered by an intact pleura without adhesions to parietal pleura. A few strong, grey-white, string-like adhesions extend across the interlobar fissure at the lung surfaces laterally; there are no adhesions between opposing pleural surfaces of upper and lower lobes. Changes in the left apex are almost identical to those on the right, although less severe. Elsewhere, pleural surfaces are smooth and glistening with deposition of pigment being essentially similar to that described in the right lung pleura. Peripheral regions of pulmonary parenchyma are almost normally crepitant and are light grey-red. Medial portions of both lobes near the hilum are more congested, less crepitant, and are dark grey-purple. Opposing pleural surfaces anteriorly display patchy, irregular, subpleural, dark red-purple foci which occasionally are confluent.

Palpation of both hilar regions discloses numerous firm, rounded, subpleural nodules along the courses of bronchi. These nodules are formed mainly by enlarged, congested or hemorrhagic lymph nodes; many nodes along the secondary and tertiary bronchi measure more than 1.0 cm in diameter. Bronchi to all lobes arise normally and follow usual courses. The lining epithelium is dark grey-red; many smaller bronchi contain soft, grey, translucent mucoid material. Pulmonary arteries and veins are dilated and contain dark red-black blood. Several vessels contain firm friable clots but all separate easily from the underlying endothelium, leaving smooth, glistening, grey-yellow surfaces; these clots have characteristics indicating post mortem origin.

D. LYMPHATIC AND HEMATOPOIETIC SYSTEMS

1. Lymph nodes: The most striking findings in this autopsy examination involve changes in lymph nodes of the neck and thorax. Lymph nodes elsewhere in the body are minimally altered. The approximate location and size of nodes associated with the tracheobronchial tree are diagrammatically shown in Figure 7.

Nodes of the anterior cervical group are numerous over the anterior surfaces of the larynx and trachea, along anterior jugular veins, and among veins of the thyroid plexus. These nodes are generally discrete, oval, dark red-brown, and measure from 0.3 to 1.0 cm. Their capsules are thin and regular. Nodes measuring less than 1.0 cm lie in clusters at the lower poles of the thyroid gland in edematous soft tissues among dilated veins of the thyroid plexus.

Deep cervical nodes are numerous in both the superior and inferior chains. About the pharynx, esophagus and trachea these nodes are closely associated with dilated veins and lie in groups of five to six nodes. The largest nodes at the base of the neck are 1.5 cm in diameter and have firm, dark-red cut surfaces; capsules appear intact and are of uniform thickness.

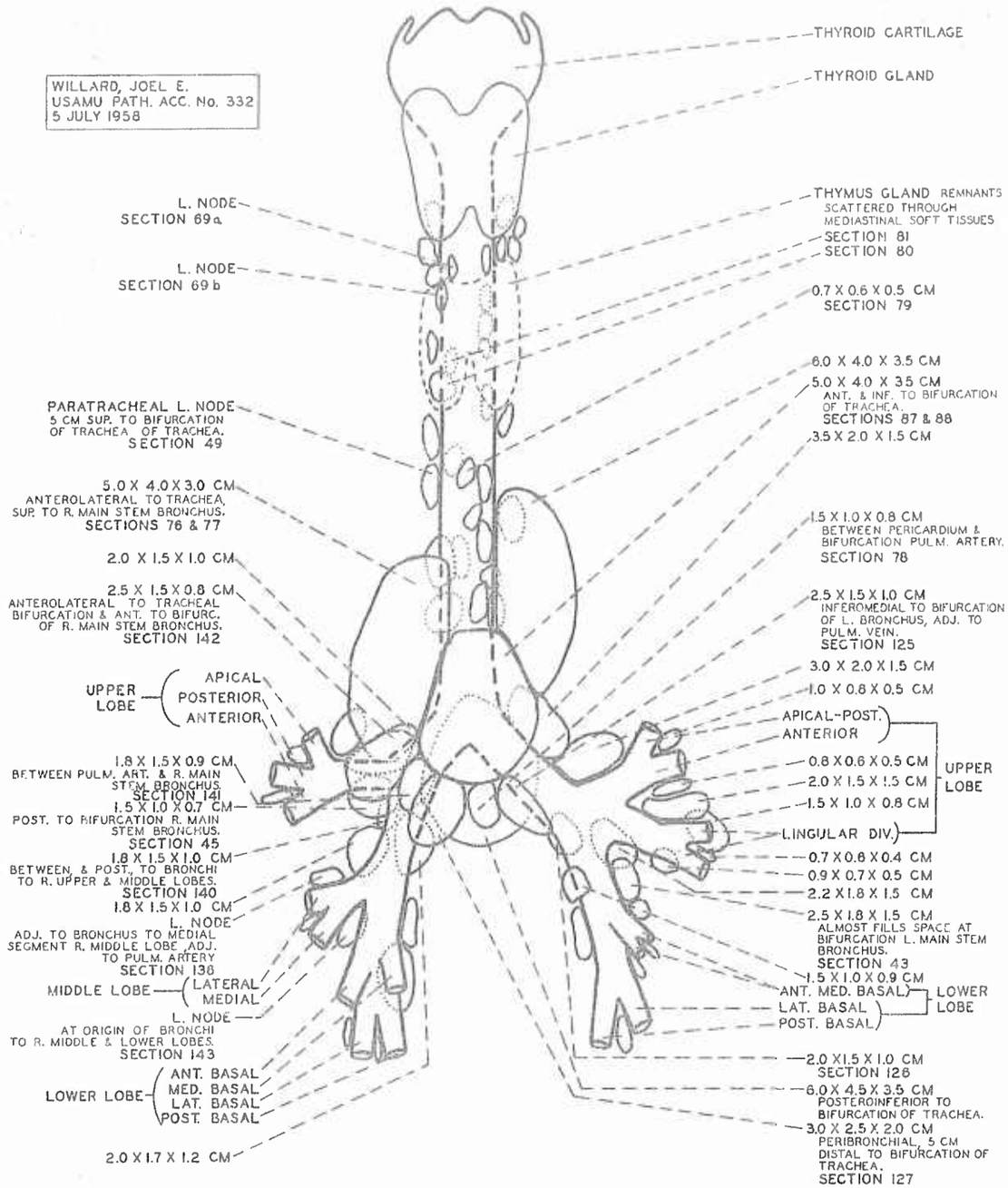

FIGURE 7. TRACHEOBRONCHIAL LYMPH NODES.
DIAGRAM OF APPROXIMATE SIZES AND DISTRIBUTION.

Tracheobronchial nodes are tremendously enlarged, firm, congested and hemorrhagic (Figures 8 and 9). Larger paratracheal and bronchial nodes are often fused into dark reddish-purple masses. Right paratracheal nodes form a mass measuring 8.0 cm in vertical diameter and reaching superiorly to the level of the first rib. Medially, this mass is molded about the trachea and esophagus; laterally it bulges under the parietal pleura to form a relatively smooth and regular surface with a slightly curved but almost vertical margin. This single large mass is easily separated by blunt dissection into several parts, each measuring 5.0 cm or less at greatest diameter. These component masses cannot be further divided without tearing the friable, firm, hemorrhagic tissues, although the appearance of cut surfaces suggests that each mass is composed of multiple smaller nodes. Inflammatory and hemorrhagic processes appear to have extended diffusely through the capsules of many individual nodes so that the identity of specific structures is almost completely lost. Multiple sections disclose several, scattered, discrete, 1.0- to 2.0-mm foci of calcification through this mass of nodes. Calcification is most marked at a level 4.0 cm superior to the tracheal bifurcation, 0.5 cm beneath the node capsule, in an irregular region measuring 1.0 cm in diameter. Aggregates of lymph nodes along the left of the trachea form a mass measuring 10.0 cm vertically; it is quite similar in appearance and consistency to the mass on the right, and extends upward to the first intercostal space. Smaller aggregates and individual nodes lie among larger masses and are numerous along the esophagus, great vessels and trachea. Bronchial nodes form two main masses; one is irregularly round, measures 5.0 x 4.0 x 3.5 cm, and is molded over the anteroinferior aspect of the tracheal bifurcation; it almost completely fills the space between right and left bronchi. The other lies in the corresponding posterior position; it measures 6.0 x 4.5 x 3.5 cm, with a vertical long axis. One surface of this node is molded about the wall of the esophagus; there is no clear demarcation between the capsule of the node and the outer layers of the esophageal wall. Sections disclose minute foci of calcification scattered through central areas of both nodes; cut surfaces are dark brown or red-black, firm, and almost devoid of normal architectural features. Many bronchopulmonary nodes are molded or are merged with large bronchial nodes. About the main stem bronchi the largest nodes of this group measure 2.5 to 3.5 cm. Numerous smaller nodes are discrete, dark red-black and fill spaces between secondary bronchi and major blood vessels. Many of these nodes cut with a gritty sensation and contain large amounts of black pigment. These nodes often cause bulging of overlying pleura and account for the nodules felt on palpation of the hilar regions. At several sites it is not possible to separate the nodes from adjacent bronchi without tearing tissues; at these points the capsules of nodes are indistinct; firm, grey-black surfaces of the nodes merge with congested peribronchial tissues. Sections of a 2.0 x 1.5 x 1.0 cm node on the anterosuperior aspect of right upper lobe bronchus disclose a sharply demarcated, central, bright grey-yellow, friable region of partial calcification measuring 0.7 x 0.5 x 0.4 cm. Pulmonary nodes measuring up to 1.0 cm are numerous about the secondary and tertiary bronchi.

Anterior mediastinal nodes are generally less enlarged than those of the tracheobronchial group, but many nodes about the arch of the aorta and its branches measure 1.5 cm in diameter. Some of these nodes lie in groups of two to three, and fusion is rarely seen. Scattered among thymic remnants and adjacent edematous soft tissues are numerous discrete, firm, red-brown nodes measuring less than 1.0 cm in diameter.

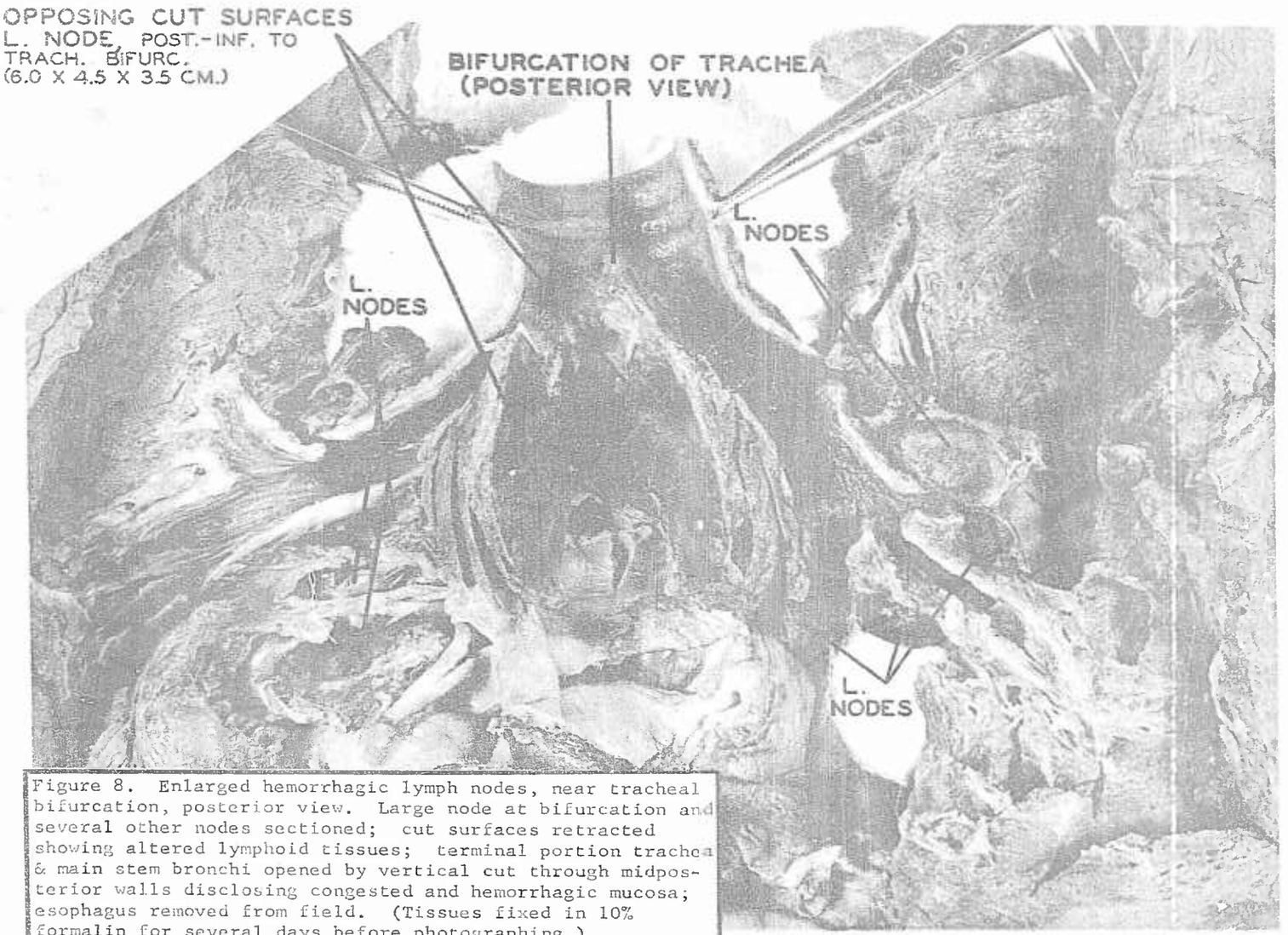

Figure 8. Enlarged hemorrhagic lymph nodes, near tracheal bifurcation, posterior view. Large node at bifurcation and several other nodes sectioned; cut surfaces retracted showing altered lymphoid tissues; terminal portion trachea & main stem bronchi opened by vertical cut through midposterior walls disclosing congested and hemorrhagic mucosa; esophagus removed from field. (Tissues fixed in 10% formalin for several days before photographing.)

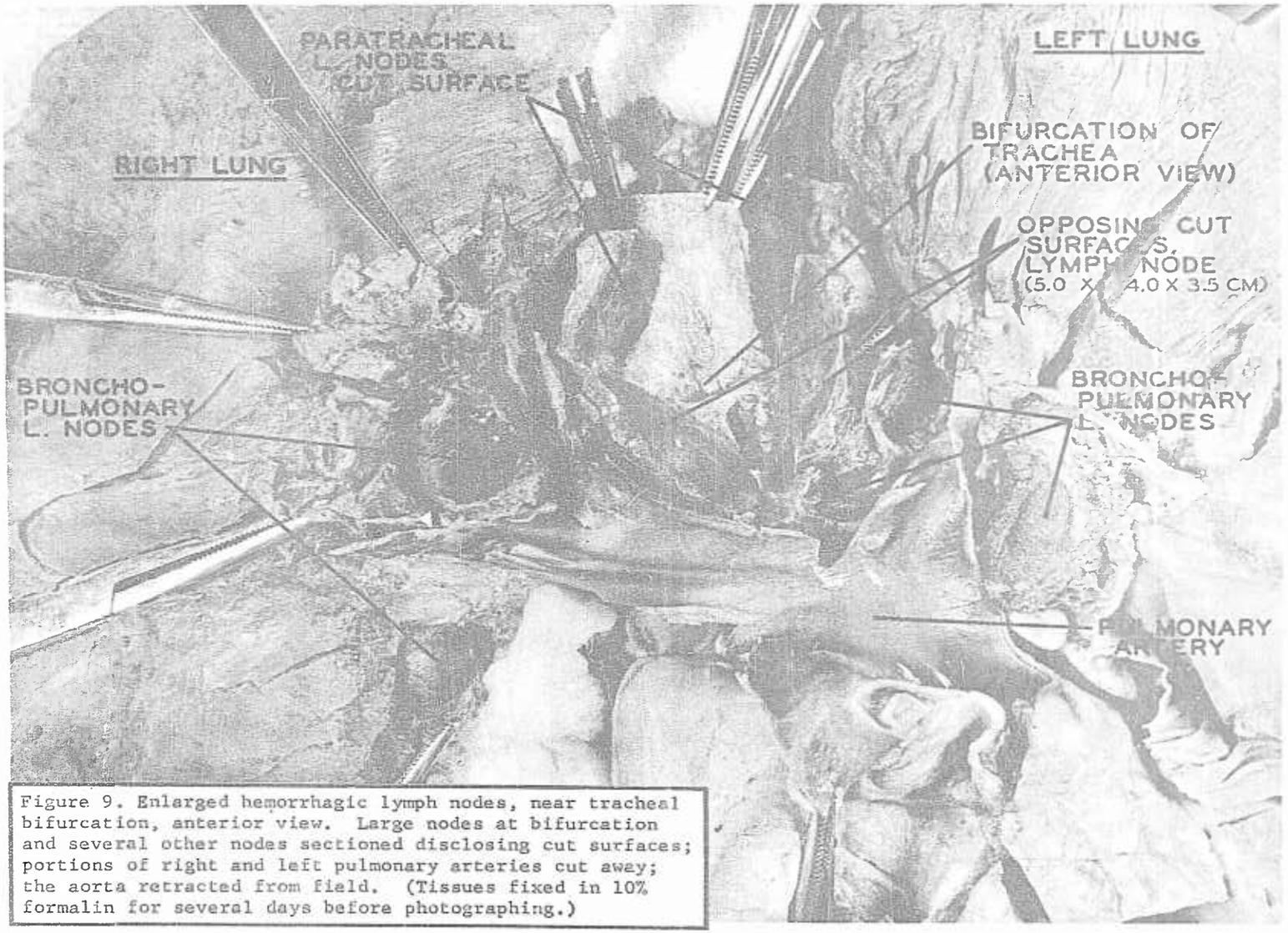

Figure 9. Enlarged hemorrhagic lymph nodes, near tracheal bifurcation, anterior view. Large nodes at bifurcation and several other nodes sectioned disclosing cut surfaces; portions of right and left pulmonary arteries cut away; the aorta retracted from field. (Tissues fixed in 10% formalin for several days before photographing.)

Posterior mediastinal nodes are found without difficulty but are less numerous than tracheobronchial nodes. The relatively few nodes found near the diaphragm along the esophagus and descending aorta are discrete, oval, dark red-brown and measure up to 1.0 cm in diameter. All these nodes have tense, thin, regular capsules.

Sternal, intercostal and diaphragmatic nodes are examined at only a few sites. These nodes all measure less than 1.0 cm in diameter, are discrete and have grey-brown cut surfaces and tense smooth capsules.

Parietal nodes of the abdomen and pelvis are slightly enlarged but nowhere display the striking changes seen in the tracheobronchial groups. Occasional oval, discrete, grey-brown nodes measuring less than 1.0 cm lie along the iliac, epigastric and hypogastric vessels. Nodes of the lumbar group associated with the abdominal aorta are more numerous, darker red, and slightly larger. None of these nodes is adherent to adjacent structures; capsules are intact, thin, and regular.

Visceral nodes of the abdomen are slightly enlarged and congested but no focal lesions or hemorrhages are detected. Most of these nodes are approximately 0.5 cm in diameter; a few measure 1.0 cm. Occasional nodes lie along the curvatures of the stomach, the common bile duct, splenic artery and about the pancreas. Nodes are numerous along major vessels in the mesenteries of the small and large intestines, and along lines of attachment to the bowel.

Nodes draining distal portions of the extremities are examined only by external palpation; significant lymphadenopathy is not found. In the axillary and inguinal regions, along the courses of major vessels, there are a few scattered, discrete, oval, slightly enlarged, firm but freely movable grey-brown or grey-red nodes.

Occipital, auricular, and facial lymph nodes are not examined; none are felt on palpation.

The thoracic duct is not remarkable in its terminal portions; the abdominal and lower thoracic courses of this vessel are not examined.

2. Spleen: This organ weighs 161 gm and measures 10.5 x 9.5 x 4.0 cm. The phrenicolienal ligament is soft and pliable; it contains normal lienal vessels. Two accessory spleens lie in the firm, bright yellow, fatty tissue of the gastrolienal ligament; the larger measures 2.5 x 2.0 x 2.0 cm; the smaller measures 0.7 x 0.6 x 0.6 cm. In the hilum of the main organ, adjacent to major vessels, are three oval, firm, dark red-brown lymph nodes measuring from 2.0 x 4.0 to 3.0 x 5.0 mm in greatest diameter. Sections disclose intact capsules and soft, moist, red-brown cut surfaces. Splenic capsules are greyish-purple, uniformly thin and slightly wrinkled. An irregular, oval, tan, slightly elevated lesion lies on the midanterior margin of the main organ 5.0 cm from the hilum; it measures 1.3 x 1.4 cm. Sections through the lesion disclose a 0.6 x 0.5 x 0.8 cm cystic space immediately beneath the splenic capsule; it contains a translucent, grey, semisolid material resembling mucus and has a smooth greyish-yellow lining; the cyst wall is firm, grey and measures from 0.5 to 1.0 mm.

A 3.0 x 4.0 cm dark red-brown subcapsular area lies on midsuperior surface. Cut surfaces of the main organ and the two accessory spleens are uniformly greyish-red, soft and friable; except for fibrous trabeculae, architectural landmarks cannot be identified with certainty; no focal lesions are seen.

3. Thymus: This structure is atrophic and its margins cannot be delineated with certainty. Scattered through the edematous and congested soft fatty tissues immediately beneath the sternum are firm, tan or grey-yellow regions with an appearance characteristic of thymic remnants. These are found from the level of the upper pericardium into the lower neck. Some foci cut with a gritty sensation.

4. Bone Marrow: Sections across three lumbar vertebrae and the sternum at two levels disclose uniformly dark red-brown marrow. Red-black blood oozes from sawed surfaces. Bone trabeculae are delicate and have normal arrangement and consistency. Sections of two ribs across their junctions with costal cartilages disclose normal marrow cavities. Cut surfaces are softer, less congested, and appear to contain more fat than the vertebral marrow.

E. CARDIOVASCULAR SYSTEM

1. Heart: The heart is not weighed; it is removed as part of a single block specimen including other mediastinal structures and the lungs; its estimated weight is 275 gm. Position, size, and conformation are normal. A needle puncture wound thru the anterior surface of the left ventricle lies 1.5 cm to the left of the interventricular septum. Elsewhere, epicardial surfaces are smooth and glistening; subepicardial fat is not remarkable. Both atria and the venae cavae are moderately dilated. All heart chambers contain red-black blood; firm friable clots lie in the apices of both ventricles, among trabeculae carneae, and in the atrial appendages. These clots are easily separated from the endocardium, which is smooth, glistening and light grey-yellow in all chambers. The fossa ovalis measures 1.0 x 0.8 cm and is anatomically closed, although a slit-like opening at its upper margin leads partially thru the atrial septum. The aortic valve measures 7.8 cm; bicuspid, 11.0 cm; pulmonic, 8.0 cm; and tricuspid, 11.5 cm. The myocardium at the base of the papillary muscles is 1.1 cm thick for the left ventricle and 0.3 cm, for the right ventricle. Musculature of the atrial walls varies from 0.15 to 0.3 cm in thickness.

The right atrium receives the superior and inferior venae cavae and the coronary sinus in the usual fashion; pulmonary veins enter the left atrium normally. Pectinate muscles of the atria are not remarkable. Chambers of the right and left ventricles have normal volumes and contours; the papillary muscles and trabeculae carneae are not unusual. Multiple sections of both ventricles and the interventricular septum disclose uniformly firm, light red-brown surfaces.

Cusps of the tricuspid valve approximate normally, and are thin, translucent, freely movable and smooth. Chordae tendineae are delicate and thread-like. There is a slight increase in nodularity and thickness along the margins of the ventricular surfaces. Cusps of the bicuspid valve are similar to those of the tricuspid valve, except that thickening of the free margins is slightly more marked. Also, in several areas of its anterior cusp there are irregular, focal,

light grey-yellow regions which are firmer and less flexible than adjacent areas. None of these changes is considered capable of significantly altering normal function.

Pulmonary and aortic valve cusps approximate evenly and completely. Each cusp is attached normally, has smooth margins, and moves freely. Corpora arantii and adjacent areas are very slightly thicker than normal; there is a slight increase in thickness near the lines of attachment but no adhesions exist between the valve cusps and the lateral walls of the sinuses of Valsalva. These minor alterations are more noticable in the aortic valve than in the pulmonary. None of these changes is sufficiently advanced to impair function significantly.

Both coronary arteries arise normally, divide into the usual branches, and follow normal courses. Both coronary ostia are slightly irregular due to minimal sclerotic changes, but are of normal diameter and lie below the level of the free margins of the aortic cusps. No occlusion is found in major branches of the coronary vessels. The intimal surfaces are smooth and of normal color except in a few focal areas of minimal atherosclerosis near the origins of major branches. Coronary veins display no noteworthy features except moderate dilation.

2. Pulmonary Vessels: No abnormalities are detected in the origin or course of the pulmonary artery or its right and left branches. The pulmonary artery diameter is uniform and measures slightly less than 3.0 cm. Firm dark red-black clots can be teased without difficulty from most branches of the pulmonary arteries as they enter the lungs. These clots appear to be casts of vessel lumina. Intimal surfaces are everywhere smooth and light grey-yellow except for a few irregular foci which are slightly firmer and more yellow than adjacent areas. The ligamentum arteriosum follows its usual course between the aortic arch and the left pulmonary artery. It is 3.0 cm long; the inferior half is completely occluded, measuring 0.3 cm in diameter. It is a tough, non-elastic, fibrous cord; a 1.0 mm probe can be passed easily thru the persistent opening in the aorta to the midpoint of the ligamentum arteriosum. Pulmonary veins are normally formed, follow usual courses, and have smooth glistening intimal surfaces; these veins are dilated and contain red-black blood. A few cast-like clots are teased from the lumina of veins near the hilar regions of the lungs. Numerous vessels of the pulmonary system are in close relation to markedly enlarged tracheobronchial lymph nodes; at many sites the inflammatory and hemorrhagic processes in nodes appears to extend to the vessel walls, but occlusion of the lumina at these points is not demonstrated, nor are thrombi seen attached to intimal surfaces at affected sites.

3. Aorta: The aorta arises normally, has the usual relations with other structures throughout its course, and is only slightly decreased in elasticity. The circumference of the ascending aorta is 7.5 to 8.0 cm; at the diaphragm the descending aorta has a circumference of 5.0 cm; the abdominal aorta, 4.0 cm immediately above its bifurcation. A few scattered intimal atherosclerotic plaques are found at all levels, but none of the lesions is far advanced and multiple sections fail to disclose calcification. For the most part, the intimal surface is smooth, glistening and light grey-yellow.

4. Systemic Arteries and Veins: No anomalies are noted in the origin of any major branches of the aorta. Barely detectable atherosclerotic plaques are seen in several larger arteries near points of origin, but the arterial system generally is not remarkable.

Generalized congestion is the most striking vascular abnormality. Stasis is most marked in veins of the chest, neck and head. Sections across veins in these areas disclose dilated lumina filled with red-black, non-clotted blood. Endothelial surfaces are smooth, grey-yellow, and glistening; thickening of vessel walls is not seen. The appearance of blood vessels at specific sites and within organs is described under the discussions of individual organs. Thrombi are not found in the iliac vessels, nor in other major veins or arteries. Arteries and veins of the extremities are not dissected.

F. GASTROINTESTINAL SYSTEM

1. Mouth: The lips are not remarkable except for cyanosis of the intact mucous membranes. The dark grey-purple oral mucosa is intact and smooth. No artificial dentures are present. Several teeth contain metallic restorations. The first upper right premolar tooth (R-5) is absent; the socket is healed, clean, and shows no evidence of infection. The gums are firm and not unusual except for slight recession of the gingival margins, especially at the buccal surfaces of the incisor and premolar teeth. Abnormalities are not detected in the hard or soft palate. The uvula is not remarkable except for moderate congestion and edema. The tongue is bilaterally symmetrical, firm, and covered by intact mucosa; its papillae and frenulum linguae appear normal. Salivary glands are normal to palpation; dissection is not performed. Glossopalatine and pharyngopalatine arches are bilaterally symmetrical and are covered by intact, smooth, congested mucosa. Palatine tonsils are small, have the usual crypts on medial surfaces, and show no surface ulcerations or exudate.

2. Pharynx: The pharyngeal mucosa is dark grey-purple; no ulcerations or exudate are seen. It is smooth except for multiple, 1.0 to 2.0 mm, slightly elevated, focal areas on the posterior wall in the nasal and oral portions; these areas have an appearance suggesting aggregates of lymphoid tissue. Several, dark red, irregular, 1.0- to 5.0-mm focal areas in the region of the aryepiglottic folds have an appearance suggesting intense congestion or submucosal hemorrhage.

3. Esophagus: The origin and course of the esophagus are normal. The empty lumen is lined by moderately congested and edematous mucosa thrown into the usual longitudinal folds. The mucosal surface has a varied but generally ragged appearance with grey-red grandular areas intervening between smooth grey-white regions. The appearance suggests loss of surface epithelium and intense submucosal stasis in multiple, irregular focal areas. Deeper layers of the wall are congested and edematous, particularly in the thoracic portion. At several points tremendously enlarged paratracheal or bronchial lymph nodes lie in intimate contact with the anterolateral esophageal walls. In these areas the inflammatory and hemorrhagic processes in the lymph nodes appear to extend into the musculature of the esophagus.

4. Stomach: Cardiac and pyloric orifices are not unusual. The lumen contains a small amount of gas and 15 to 20 ml of grey-green, mucoid material. Peritoneal surfaces are smooth and glistening; dilated grey-pink, subserosal blood vessels are prominent. The mucosa forms low rugal folds; it is moderately congested and edematous; dark red focal areas contrast with adjacent more normally appearing regions. Ulcerations are not seen. Muscle layers are normally developed.

5. Small Intestine: The duodenum originates normally at the pylorus; all four portions lie in their usual positions and have normal relations with adjacent structures. Pancreatic and common bile ducts appear normal and enter the duodenum characteristically through the medial wall of the descending portion. Areas of the duodenum covered by peritoneum have smooth glistening surfaces. The mucosa is moderately edematous and congested. Focal areas of the mucosal surface in the superior portion near the pylorus are irregular, mottled grey-green and grey-brown, with a granular appearance suggesting loss of covering epithelium. Small amounts of grey-green mucoid material occupy the lumen. Muscles of the wall are not remarkable.

A single 2.0 x 1.5 cm, fairly well, demarcated lesion, in the wall of the jejunum lies 140 cm distal to the duodenojejunal flexure. The lesion is situated in that portion of the gut wall opposite the line of mesenteric attachment. In this area the serosa is dark red, rough, firm, and covered by a granular grey-red friable material; the mucosal surface is dull grey-red and opaque, and the wall is two to three times normal thickness; normal architectural detail is lost in all layers of the wall. Elsewhere in the jejunum and ileum the serosal surface is smooth and glistening; the mucosa is slightly congested and edematous; musculature is not remarkable. Peyer's patches are identified without difficulty, but specific focal lesions or ulcerations are not detectable in the covering mucosa nor in cut surfaces of lymphoid aggregates. The lumen contains very little gas; small amounts of bile-stained, thick, mucoid material adhere to mucosa. The mesentery is normally formed, contains the usual amount of firm bright-yellow fat, and is thin, translucent, and freely movable. Mesenteric veins are moderately dilated and contain dark red, non-clotted blood; no thrombi or emboli can be demonstrated. Numerous lymph nodes lie in the mesentery along courses of major blood vessels and near the line of attachment to the intestine. These nodes are discrete, have grey-brown or grey-yellow cut surfaces and are oval or flattened; most of them measure 0.3 to 0.5 cm in greatest diameter; a few measure 1.0 cm. The contrast in appearance and consistency between these relatively normal nodes and those of the mediastinum is striking.

The appendix measures 14 cm in length and from 0.5 to 0.7 cm in diameter, being narrowest in its distal half. It curves laterally and posteriorly about the cecum and is tightly bound in a mass of fat and firm, grey-white connective tissue to the posterolateral cecal wall. The lumen is 1.0 to 3.0 mm in diameter in the proximal portion and contains firm, semisolid, brown fecal material, near the tip, the lumen is completely obliterated by firm white tissue; various layers of the wall cannot be identified with certainty.

6. Large Intestine: The ileocecal valve is not remarkable. Serosal surfaces of the colon are smooth and shiny. Taeniae coli are normal. Appendices epiploicae contain normal, firm, yellow fat. The lumen is moderately dilated with gas and contains small amounts of semisolid, grey-brown material and dark greenish-brown mucoid material. The mucosa is grey-red and appears slightly congested and edematous. Focal lesions are not found. The rectum is more congested than the colon, and in its terminal portion the mucosa is rough, granular and mottled grey-red. Transition from rectum to anus is normal. Several submucosal dilated veins are prominent approximately 1.5 cm above the anal opening. No thrombosed veins or sites of mucosal ulceration are demonstrated.

7. Liver and Gall Bladder: The liver is normal in size, consistency, ligamentous attachments, position, and relation to adjacent structures; it weighs 1,220 grams. Peritoneal surfaces are smooth, glistening and red-brown; the capsule is thin, of uniform width and regular. Cut surfaces are dark red-brown and similar in all regions. Large veins are filled with dark-red, non-clotted blood. Lobular structure is easily identified; central regions are darker than lobular peripheries. The hepatic duct is formed normally, is patent throughout its course, contains light yellowish-green bile, and is lined by smooth bile-stained mucosa. The gall bladder occupies its usual position and has a smooth, glistening, dark greenish-brown serosal surface. It measures 11 cm in length and 3.0 cm in diameter, at the widest portion of the fundus. The lumen contains approximately 10.0 ml of thick, mucoid, dark green-brown bile, and four stones. Measurements of stones are: 2.0 x 1.6 x 1.5 cm; 1.8 x 1.6 x 1.4 cm; 0.7 x 0.5 cm; and 0.6 x 0.5 cm. The two larger stones are irregularly oval; surfaces are rough and mottled grey-brown or dark green. Interiors are almost entirely crystalline and composed predominately of light grey-yellow or white translucent brittle material. Regions with laminated structure alternate without definite arrangement with areas having radiations of crystals from the center. Dark brown-black areas are more numerous near the centers. The appearance is characteristic of mixed stones containing mainly cholesterol with lesser amounts of calcium bilirubinate and carbonate. The two smaller stone are irregular, crumbling easily into small fragments, light grey-yellow, and composed mainly of cholesterol. The mucosa is darkly bile-stained, velvety and smooth except in the areas opposite stones, where the surface is granular, firm, and mottled grey-red or grey-green. Cystic, hepatic and common bile ducts are normally formed, patent, of the usual diameters, and lined by smooth lightly bile-stained mucosa. No stones or other objects are found in the lumina of these ducts, nor do lymph nodes or other masses narrow them by external pressure.

8. Pancreas: Position, consistency, color and relationship of the pancreas to adjacent structures are normal. It measures 15.0 cm in length and in its eliptical cross section, 4.0 x 2.0 cm at the largest point. It weighs 110 gm. Cut surfaces disclose normal lobular structure, dilated veins, and a duct system with no abnormalities. Islets of Langerhans are questionably identified as minute glistening grey dots. The pancreatic duct enters the duodenum in the usual fashion; it is lined by intact, smooth, light grey-yellow mucosa, and is patent throughout its course.

G. GENITOURINARY SYSTEM

1. Kidneys: The right kidney weighs 140 gm and measures 10.5 x 6.0 x 4.0 cm; the left kidney weighs 150 gm and measures 11.5 x 5.5 x 4.0 cm. Renal fascia and perirenal fat appear normal. Renal blood vessels and ureters lie in normal positions. Both renal capsules are uniformly thin and regular, and strip easily from smooth dark-red cortical surfaces. A solitary cyst projects 1.5 cm above the midposterior surface of the right kidney; it measures 3.0 x 2.5 x 1.5 cm and extends from the level of the hilum toward the upper pole. This multiloculated thin-walled cyst contains clear, serous, straw-colored fluid and has a smooth grey-white lining; it extends thru the kidney from the capsule to the renal pelvis at its widest point. Cut surfaces of both kidneys display no abnormalities except accentuation of vascular markings due to moderate stasis. Cortical thickness varies from 4 to 6 mm. The renal pelves and calyces have normal contours, and lining mucosal surfaces are smooth, grey-white and glistening.

2. Ureters: Both ureters arise normally, pursue normal courses to the bladder, and are of normal diameter. Lining mucosal surfaces are smooth and grey-white. Musculature is not remarkable.

3. Bladder: The bladder contains 400 ml of clear, yellow urine. No abnormalities are detected in its smooth glistening, peritoneal surface or muscular wall. Orifices of the urethra and ureters appear normal. No focal lesions are seen in the smooth grey-white mucosa of the fundus. Dilated, small, superficial, mucosal blood vessels are prominent, especially in the inferior portions of the bladder wall. Scattered, 1.0- to 4.0- mm, red-brown foci of stasis or hemorrhage are numerous in the submucosa of the posterior wall inferiorly. In some poorly demarcated sites the mucosal surface is granular and a dull grey-brown. A triangular, dark red-brown area of mucosal hemorrhage or intense stasis extends posteriorly from the urethral orifice; it measures 3.5 x 2.5 cm and includes the trigonum vesicae.

4. Urethra: The prostatic and membranous portions of the urethra have normal diameters and are lined by intact grey-white mucosa except for scattered, ill-defined, mottled, dark grey-red regions. The cavernous portion of the urethra is not dissected; palpation discloses no abnormalities.

5. Reproductive Organs: Abnormalities are not detected in the wall of scrotum. Both testes are covered by a smooth grey-white tunica albuginea of normal thickness and consistency, and with no evidence of adhesions to the tunica vaginalis. Neither scrotal sac contains excess fluid. The left testis measures 5.5 x 4.0 x 2.5 cm and the right testis, 5.0 x 3.0 x 3.0 cm. Sections of both testes disclose uniform, tan-brown, friable, softer than normal parenchyma which bulges slightly above the capsules. The tubules string-out less than normal.

Epididymes lie in the usual positions and appear normal externally. Cut surfaces are not remarkable except for slight dilatipn of tubules in the superior portion, where there are multiple small cysts, measuring from 1.0 to 3.0 mm; most of these spaces contain thick, translucent, grey, mucoid material;

some are filled with more solid grey-white material and cut with a gritty sensation. From each epididymis the ductus deferens arises normally and follows its usual course. Multiple sections of the spermatic cords disclose no abnormalities except dilated tortuous veins of the pampiniform plexuses; at several points venous channels are occluded by solid dark grey-red or grey-white masses with the appearance of thrombi in various stages of organization. Both seminal vesicles are normally situated and participate normally in the formation of the ejaculatory ducts. The right seminal vesicle measures 4.0 x 3.0 x 2.0 cm; the left gland is slightly larger, due to dilation of several tubules to form cystic spaces measuring 0.5 to 1.0 cm in diameter; these cysts contain grey, translucent semisolid material. Multiple sections disclose occasional foci of dark yellow-brown pigmentation. The ejaculatory ducts display no unusual features.

The prostate is slightly enlarged; it measures 3.8 cm vertically, 5.0 cm transversely, and 3.5 cm in greatest anteroposterior diameter. The intact capsule is of uniform thickness. Most surface areas are smooth and regular. On the midposterior surface, immediately above the origin of the membranous urethra, a firm rounded, poorly demarcated, 1.0-cm nodular area projects 5.0 mm above the adjacent surfaces. Veins of the periprostatic plexus are dilated, tortuous, and thrombosed at several points. A hard, oval, grey-yellow nodule measuring 5.0 x 4.0 x 3.0 mm projects from the wall of a large vein on the right posterolateral surface of the gland; sections disclose foci of calcification. A dark red-brown, 5.0 x 3.0 mm nodular mass in a dilated vein on the left mid-posterolateral aspect of the prostate gland appears to be an organizing thrombus. Multiple cut surfaces of the prostate at all levels exhibit a normal appearance in most regions. A few nodular foci in central portions of the gland have ill-defined margins, measure 3.0 to 6.0 mm, and are composed largely of firm, rubbery, grey-white tissue; other nodules have a honeycombed appearance, measure 3.0 to 7.0 mm and are grey-tan or grey-yellow. Some areas in the lateral lobes contain 3.0- to 6.0-mm cystic spaces filled with thick, grey, translucent material. A few regions cut with a gritty sensation suggesting the presence of corpora amylacea.

H. ENDOCRINE SYSTEM

1. Pituitary Gland: The pituitary gland is normal in size, contour, consistency and appearance. It lies normally in the sella turcica and joins the hypophyseal stalk in the usual fashion. Sections disclose a thin regular capsule of uniform width and grey-pink cut surfaces with no abnormalities except slight congestion.

2. Thyroid Gland: The weight of this gland is not determined; it is removed as part of single block specimen with the larynx and the upper third of the trachea. The left lobe measures 5.0 cm vertically, 3.0 cm transversely, and 2.5 cm anteroposteriorly; the right lobe measures 5.5 cm vertically, 2.8 cm transversely, and 2.5 cm anteroposteriorly. The isthmus is slightly irregular but is not unusual in consistency or appearance; it averages several millimeters in thickness and measures 0.8 cm in greatest vertical dimension. A poorly demarcated irregular nodule measuring 1.0 x 1.5 x 0.9 cm projects slightly above the adjacent surfaces of the left lobe in the midportion of its posterolateral margin. The capsule over the entire gland in uniformly thin

and regular. Cut surfaces in all regions of both lobes, including the nodule, are red-brown, firm, and have the usual waxy appearance; supporting connective tissue forms delicate grey-white lines. Venous plexuses over the posterior and lateral surfaces of the gland are markedly dilated and contain dark red-black blood or clots. Firm friable clots in tortuous widened veins at the lower pole of the left lobe and near the right lower parathyroid gland have an appearance suggesting the possibility of ante mortem thrombosis. These veins are closely associated with aggregates of small, dark red, firm lymph nodes.

3. Parathyroid Glands: These structures are identified at the superior and inferior poles of both thyroid lobes. Measurements are: left upper gland, 9.0 x 5.0 x 3.0 mm; left lower gland, 6.0 x 4.0 x 3.0 mm; right upper gland, 8.0 x 4.0 x 3.0 mm; right lower gland, 5.0 x 4.0 x 3.0 mm. All four glands are irregularly oval; they are covered by a smooth uniformly thin capsule and have yellowish-brown cut surfaces. All lie immediately adjacent to the thyroid capsule but are easily separated from it by blunt dissection. Several small congested lymph nodes lie near the lower parathyroid glands among dilated veins.

4. Adrenal Glands: The right adrenal gland weighs 1.6 gm; it appears smaller than normal and measures 4.0 x 3.5 x 1.5 cm. It lies in normal position. Dissection of pericapsular fat causes one margin to burst open, with a cleavage plane near the corticomedullary junction. The medulla is soft, friable, and dark grey-brown with irregular, minute, dark red foci. The cortex is grey-tan, fairly regular in width, averaging about 2.0 mm, and is firmer than the medulla. Pigment disposition in the zona reticularis can be identifded but is less distinct than usual. The capsule is not remarkable. The left adrenal gland weighs 1.4 gm, occupies its normal position and measures 5.5 x 3.2 x 1.2 cm. It is more normal in appearance than the right adrenal, having a firmer lighter grey medulla, a more yellow cortex, and an intact, uniformly thin capsule. No remarkable features are seen in periadrenal fat. Small veins in periadrenal fat and in the capsular zone are dilated.

5. Pancreas: Described in F. DIGESTIVE SYSTEM

I. CENTRAL NERVOUS SYSTEM

The brain with its attached meninges and 5.0 cm of the spinal cord weighs 1,560 gm. The dura mater has normal attachments, consistency and appearance over both hemispheres, and in its extensions, forming the falx cerebri, tentorium cerebelli, falx cerebelli, and the diaphragma sellae. Arachnoid villi are present in their usual locations and are not remarkable. The arachnoid and pia mater display no unusual features. Clear cerebrospinal fluid occupies the subarachnoid space and cisterns and the ventricular system.

Marked venous stasis is the most striking finding. External and internal cerebral veins, cerebellar veins and sagittal and other cranial sinuses are widely dilated and contain red-black, non-clotted blood. Venous lacunae near the superior sagittal sinus are also widened; parietal lacunae have indistinct margins, and the dark grey-purple appearance of the dura mater in this region suggests diffusion of blood from lacunae into the adjacent dura. All major vessels comprising the arterial system of the brain arise normally, follow normal courses, and display no abnormalities except slight and patchy arteriosclerosis.

Cerebral hemispheres are bilaterally symmetrical, and all lobes are normally formed. Gyri, fissures and sulci are not remarkable. Parallel coronal sections are made from anterior to posterior poles of the brain, at 1.0 cm intervals, and all principal structures are identified. Significant abnormalities are not detected. Consistency of tissues is normal. Lateral, third and fourth ventricles have normal contours and are lined by smooth glistening ependymal surfaces. Choroid plexuses are not remarkable. The pineal body lies in its normal position; it measures 7.0 x 5.0 mm, cuts with a gritty sensation, and consists mainly of firm grey-white tissue. Parallel sections at intervals of 0.5 cm disclose no significant alterations in the medulla oblongata, cerebellum, or proximal 5.0 cm of cervical spinal cord. Inferior portions of spinal cord are not removed. All cranial nerves arise normally, follow their usual courses to points of exit from the cranial vault, are bilaterally symmetrical, and display no abnormalities. The eyes are not removed. Structures in the inner ears are not examined.

J. MUSCULOSKELETAL SYSTEM

The skeleton is well developed and symmetrical. Abnormalities of bones, joints, or ligaments are not detected in this examination, which does not include dissection of these structures individually. Musculature of the entire body is well developed. Congestion is the only significant abnormality noted.

Fixation: Representative portions of all tissues are fixed in 10 per cent formalin.

IV. SPECIAL EXAMINATIONS

A. BACTERIOLOGICAL STUDIES

1. Post Mortem Cultures for B. anthracis.

(Dr. Martha K. Ward, USPHS; Chief, Diagnostic and Identification Branch, USAMU and Dr. Ralph E. Lincoln, Process Research Division, Fort Detrick)

Selected specimens of body fluids and tissues were cultured at the time of autopsy, July 5, for B. anthracis. Organisms when found were identified as B. anthracis by demonstration of the "string-of-pearls" reaction and gamma phagelysis, in addition to conventional procedures. Each tissue specimen consisted of several grams of the organ selected. The results follow:

SPECIMEN	RESULT
Mediastinal edema fluid (2 swabs)	Negative
Pericardial fluid (2 specimens)	Negative
Pleural fluid, right and left pleural cavities (2 specimens)	Negative
Lymph node, paratracheal, right; anterolateral to trachea, 3 cm superior to origin of main bronchus	Positive
Lymph node, paratracheal, right; 7 cm superior to bifurcation of trachea	Negative
Lymph node, anterior to bifurcation of left main bronchus	Negative
Lymph node, parabronchial, hilum of left lung	Negative
Spleen (3 specimens)	Negative
Liver (2 specimens)	Negative
Pancreas, midportion of body	Negative
Kidney, right (2 specimens)	Negative
Kidney, left (2 specimens)	Negative

SUMMARY:		
	Fluids examined	6
	Tissue specimens examined	14
	Total specimens examined	20

Original blood culture flasks of June 30 and July 1, and autopsy cultures from the right paratracheal lymph node were furnished to Dr. Lincoln, for morphological, biological, biochemical and virulence studies. He concluded that the B. anthracis isolated was a passage strain, or re-isolate of V1B stock strain under study at Fort Detrick.

2. Fluorescent Antibody Staining of Clinical and Autopsy Specimens.

(Mr. Robert F. Jaeger, Diagnostic and Identification Branch, USAMU)

a. Organism Isolated from Blood Culture (Specimen of June 30, 1958)

Smears were prepared from the blood culture bottle of June 30. Slides were air dried, fixed in absolute methanol for 10 minutes and again air dried.

Three sets of slides were stained for 30 minutes at 37°C with each of three different anti-anthrax sera, each conjugated with fluorescein isocyanate. The three antisera were:

(1) Anti-anthrax horse serum, prepared by immunization with an avirulent strain. (Dr. C. B. Thorne, Jr., Medical Bacteriology Division, Fort Detrick)

(2) Anti-anthrax rabbit serum, prepared by immunization with antigen which included capsular material. (Communicable Disease Center, USPHS, Atlanta, Georgia)

(3) Anti-anthrax rabbit sera, prepared at Fort Detrick by immunization with whole organisms of V1B strain killed by 0.5 per cent formalin. These organisms were cultured under conditions not expected to cause production of significant quantities of capsular material.

They were then washed in phosphate buffered saline (pH 7.1) for 10 minutes, with gentle agitation. Excess buffered saline was removed; cover slips were mounted in a drop of buffered glycerin. The slides were examined immediately with an ultraviolet microscope with the following results:

(1) Outlines of specifically fluorescing bacilli were seen.

(2) The intensity of fluorescence was evaluated as 2+, with fluorescence of virulent, capsulated B. anthracis organisms from suitable culture or in tissues of untreated infected animals being considered as 4+.

(3) There was a remarkable paucity of capsular material. (It should be noted that significant quantities of capsular material are rarely seen in cultures of B. anthracis grown in ordinary culture media with no provision for increased carbon dioxide tension.)

b. Examination of Tissue Imprints

Imprints were prepared from freshly cut surfaces of ten different unfixed tissues at time of autopsy. Slides were air-dried, fixed for 10 to 15 minutes in absolute methanol, air dried, held for several days at room temperature, and then stained by the same three conjugated sera. In addition, control slides were treated with normal rabbit serum, similarly conjugated with fluorescein isocyanate. The results follow:

SPECIMEN	RESULT
Lymph node, paratracheal, right, approximately 5.0 cm superior to tracheal bifurcation	Positive for specifically fluorescing bacilli. Capsular material was not demonstrated. Appearance of organisms was similar to that seen in smears from blood culture flask.
Lymph node, hilum of right lung	Negative
Lymph node, hilum of left lung (2 specimens)	Negative
Spleen	Negative
Liver	Negative
Pancreas	Negative
Kidney, right	Negative
Kidney, left	Negative
Skeletal muscle, pectoral, right	Negative
Control slides	Negative

c. Examination of Tissue Sections

Selected blocks of autopsy tissues were embedded in paraffin after fixation in 10 per cent formalin for 5 to 6 days. Sections cut at 6 to 7 microns were deparaffinized by passing through two changes of xylol, absolute, 95, 80 and 70 per cent alcohols to distilled water.

Sections from each block were stained with the conjugated horse and rabbit anti-anthrax sera and duplicate sections for controls were stained with conjugated normal rabbit serum as described previously for tissue imprints.

(1) Results of First Examination of Tissues

BLOCK NO.	SPECIMEN	RESULT
3	Spleen	Negative
26	Liver	Negative
67	Thyroid nodule, left lobe	Negative
76	Lymph node, paratracheal, right anterolateral to trachea, 3 cm above bifurcation. This block is part of node from which B. anthracis organisms were cultured.	Positive
77	Lymph node; this block and block No. 76 represent one-third of vertical section through large paratracheal node.	Positive
88	Lymph node, portion of large node filling space anterolateral to bifurcation of trachea.	Positive

Sections from identical blocks were either positive or negative with both horse and rabbit anti-anthrax sera, but organisms stained with the conjugated rabbit serum were invariably more brightly fluorescent than those seen in sections stained with horse serum. Controls were negative for fluorescent bacilli.

(2) Results of Second Examination of Tissues

Multiple sections were cut from ten selected paraffin blocks and deparaffinized as before; one set was stained with conjugated rabbit anti-anthrax serum with the following results:

BLOCK NO.	SPECIMEN	RESULT
3	Spleen	Negative
9	Spleen	Negative
48	Intestine, focal ulcerated lesion	Negative
62	Esophagus, lower third	Negative

BLOCK NO.	SPECIMEN	RESULT
76	Lymph node, paratracheal, right, 3 cm superior to bifurcation of trachea	Positive
77	Lymph node, adjacent and inferior to block No. 76	Positive
82	Lung, left, apex, apical segment	Negative
85	Lung, right middle lobe; focal nodular, hemorrhagic lesion	Positive
87	Lymph node, anteroinferior to bifurcation of trachea	Negative
139	Bronchus, to anterior segment left upper lobe, with adjacent lung and lymph node	Negative

(3) Check on Specificity of Staining

(a) A second set of sections from these ten blocks was stained with normal conjugated rabbit serum. No fluorescing bacilli were found in any section. Cover slips on slides No. 76 and No. 77 were then floated off and glycerin was removed by gentle agitation in saline. These two slides were then stained with conjugated anti-anthrax rabbit serum; specifically fluorescing bacilli could now be seen.

Following the negative result on section No. 85 after staining with conjugated normal rabbit serum, the cover slip and buffered glycerine were removed; the slide was stained with fluorescein conjugated anti-brucella (Brucella abortus) rabbit serum; no stained bacilli were seen. The cover slip and glycerin were again removed and the section stained with conjugated anti-anthrax rabbit serum; examination then disclosed outlines of specifically fluorescing bacilli. Capsular material was not seen.

(b) Another set of sections from blocks listed above was stained by the direct method with conjugated anti-anthrax rabbit sera; a duplicate set was stained by the indirect method (sections were first exposed to unconjugated anti-anthrax rabbit serum, washed, then stained with fluorescein-conjugated anti-rabbit goat serum.). Sections known to contain B. anthracis organisms were cut from tissues of an experimentally infected sheep to serve as controls.

BLOCK NO.	SPECIMEN	DIRECT STAINING	INDIRECT STAINING
	Sheep tissue controls	+	+
3	Spleen	-	+
9	Spleen	-	+
48	Intestine, focal lesion	-	-
62	Esophagus, lower third	-	-
69	Lymph node, at lower pole of thyroid, right	-	+
76	Lymph node, right para-tracheal	+	+
77	Lymph node, adjacent region to No. 76	+	+
82	Lung, left apex	-	-
85	Lung, focal lesion, right middle lobe	+	+
87	Lymph node, anteroinferior to tracheal bifurcation	-	+
88	Lymph node, region adjacent to No. 87	+	+
139	Bronchus to anterior segment, left upper lobe, with adjacent lymph node and lung	-	-
	Sheep tissue controls (stained only with goat anti-rabbit non-conjugated serum)	-	-

Additional sets of sections listed above were used to repeat the entire series of direct and indirect staining procedures. Results were the same except that sections from blocks No. 9 and No. 69 were negative instead of positive.

d. Comment

(1) Viable B. anthracis organisms were found in only one of four tracheobronchial lymph nodes cultured at time of autopsy, and only six colonies grew from approximately one gram of the single positive node. However, microscopic examination by fluorescent antibody technique and with Brown and Brenn

stain disclosed numerous bacilli with morphologic features of B. anthracis in multiple regions of the node from which the positive culture was obtained, and in several other mediastinal lymph nodes. In some sections 25 to 30 bacilli were found in one microscopic field. Although the special staining methods did not definitely establish the identity of B. anthracis, these findings suggested the possibility that at time of death many non-viable, but still physically intact, organisms were present in mediastinal tissues.

(2) Sections from ten tissue blocks, representing three lymph nodes, the spleen and the right middle lobe of lung, were shown by fluorescent antibody technique to contain organisms with morphological characteristics of B. anthracis. Failure to obtain consistent results in multiple sections from a single block may be due in part to variations in bacterial populations in different tissue regions.

(3) The absence of capsular material in organisms seen in tissue sections of this patient is an interesting and perplexing finding. It is not known whether large doses of antibiotic received by the patient caused inhibition in development of capsular material.

(4) Antisera used in these tests were not considered absolutely specific for B. anthracis. The antigenic similarity of Bacillus cereus, mycoides, megatherium and even subtilis to B. anthracis is such that specific identity of these organisms by the fluorescent antibody technique is extremely difficult. Interpretation of findings is complicated in some instances by fluorescence of nonspecific substances. Because of these factors, the demonstration of fluorescent bacilli in specimens from this patient stained by the fluorescein isocyanate-conjugated antisera is not considered unequivocal identification of B. anthracis.

3. Tests for Toxins

(Dr. Curtis B. Thorne, Jr., Medical Bacteriology Division, and Dr. Martha K. Ward, USPHS, Chief, Diagnostic and Identification Branch, USAMU, Fort Detrick)

a. Examinations to determine whether B. anthracis toxin was present in serum, pleural fluid and tissues were performed by both the agar diffusion method of Thorne and Belton[17] and the intradermal skin test method of Smith and Keppie[27].

b. Materials Tested:

(1) Serum - from blood collected on June 16, two weeks prior to onset of fatal illness and from blood collected on June 30 and July 3, the second and fifth days of clinical illness.

(2) Pleural fluid, collected at autopsy.

(3) Tissues - representative specimens from spleen, kidney and mediastinal lymph node, obtained at autopsy.

c. Preparation of Tissue Emulsions

Two samples each of spleen, kidney and mediastinal lymph node tissues, each weighing approximately one gram, were ground in Tenbroeck tissue grinders. To one aliquot was added approximately 2.0 ml of gelatine-phosphate diluent; the remaining portion of the ground specimen was mixed with 2.0 ml of the bicarbonate buffer used by Thorne for *in vitro* isolation of Fraction II of the toxin.

Since both British and American workers have demonstrated that toxin from *B. anthracis* consists of at least two fractions, neither of which is toxic when acting alone, the intradermal tests in guinea pigs were performed in this manner:

(1) Test material alone.

(2) Test material + known Fraction I of toxin.

(3) Test material + known Fraction II of toxin.

d. Results:

There was no evidence of the presence of *B. anthracis* toxin, nor of either of its known fractions, using the agar diffusion method or intradermal inoculation of guinea pigs.

B. ANALYSES OF TISSUES FOR MINERALS

(Frank B. Johnson, M.D., Chief, Histochemistry Section, AFIP,
Major Edward C. Knoblock, MSC, Chief, Department of Chemistry, WRAIR,
and Pvt. Malcolm Hendrickson, Walter Reed Army Medical Center, Washington,
and J. B. White, M.D., and J.W.M. Magee, Federal Bureau of Investigation,
Washington)

Analyses of lung and tracheobronchial lymph node tissues were requested primarily to determine whether beryllium and silicon were present in abnormal amounts. Control specimens were blocks of liver and pancreas. Tissues had been formalin-fixed. Ten per cent formalin and tap water used to prepare the fixative were submitted as control specimens.

1. Spectrographic Analyses for Beryllium (WRAMC)

a. Specimens

(1) Lung, right middle lobe; single block of tissue from region immediately medial and superior to focal hemorrhagic lesion.

(2) Lung, right middle lobe; a composite specimen, consisting of 3 blocks of tissue from the region between the focal hemorrhagic lesion and the hilum of the right lung; one block contained a hilar lymph node.

(3) Lymph node, right hilar.

(4) Control specimens known to be positive for beryllium and another known to be negative (prepared at AFIP).

(5) 10 per cent formalin solution.

(6) Tap water used in preparation of formalin fixative.

(7) Blank carbon electrodes.

b. Equipment and Procedure

(1) Specimens were ashed by pre-evaporation under a heat lamp, followed by incineration over a Bunsen burner at approximately 800°F.

(2) Ashed materials were excited and the resultant spectra were photographically recorded on a Bausch and Lomb medium quartz spectrograph plate. The spectrum region of special interest was in the ultraviolet range spanning the most sensitive line for beryllium at 2348.61 angstroms.

(3) The photographic plate used was obtained from the Eastman Kodak Company, and was developed by the method described by the manufacturer. (Plate No. 1, Spectrum Analyses, Eastman Kodak Co.)

(4) The comparison standard employed was R.U. (Raies Ultimes) powder, which contained 50 elements. (Johnson, Mathey & Company, Ltd., London).

(5) The plates were exposed at different times, but the operational techniques remained the same, except for changing control specimens. The conditions of exposure were: Slit - 1 micron; Hartman wedge, 5 mm and 3 mm; excitation - high (9-10 amperes), NSL direct current arc source; SA No. 1 plates; and 20 seconds exposure.

c. Results:

(1) Right middle lobe (one tissue block):

A positive test was obtained for beryllium: "question trace, or below 10 ppm" ("this limit is suggested for the sensitivity of beryllium, using this type technique and instrumentation"). Spectral lines marked on the positive black and white print of the photographic plate show beryllium, 2348.87 angstroms; and carbon 2478.57 angstroms (Figure 10).

(2) Lymph node, hilum of right lung - negative for beryllium.

(3) Comment:

Other noticeable lines are due to mineral content of the tissue, mainly iron, and to impurities of the graphite electrodes (not pronounced in the positive print, but detectable in the negative). The dispersion of the prism spectrograph in the spectral region is approximately 30 angstroms

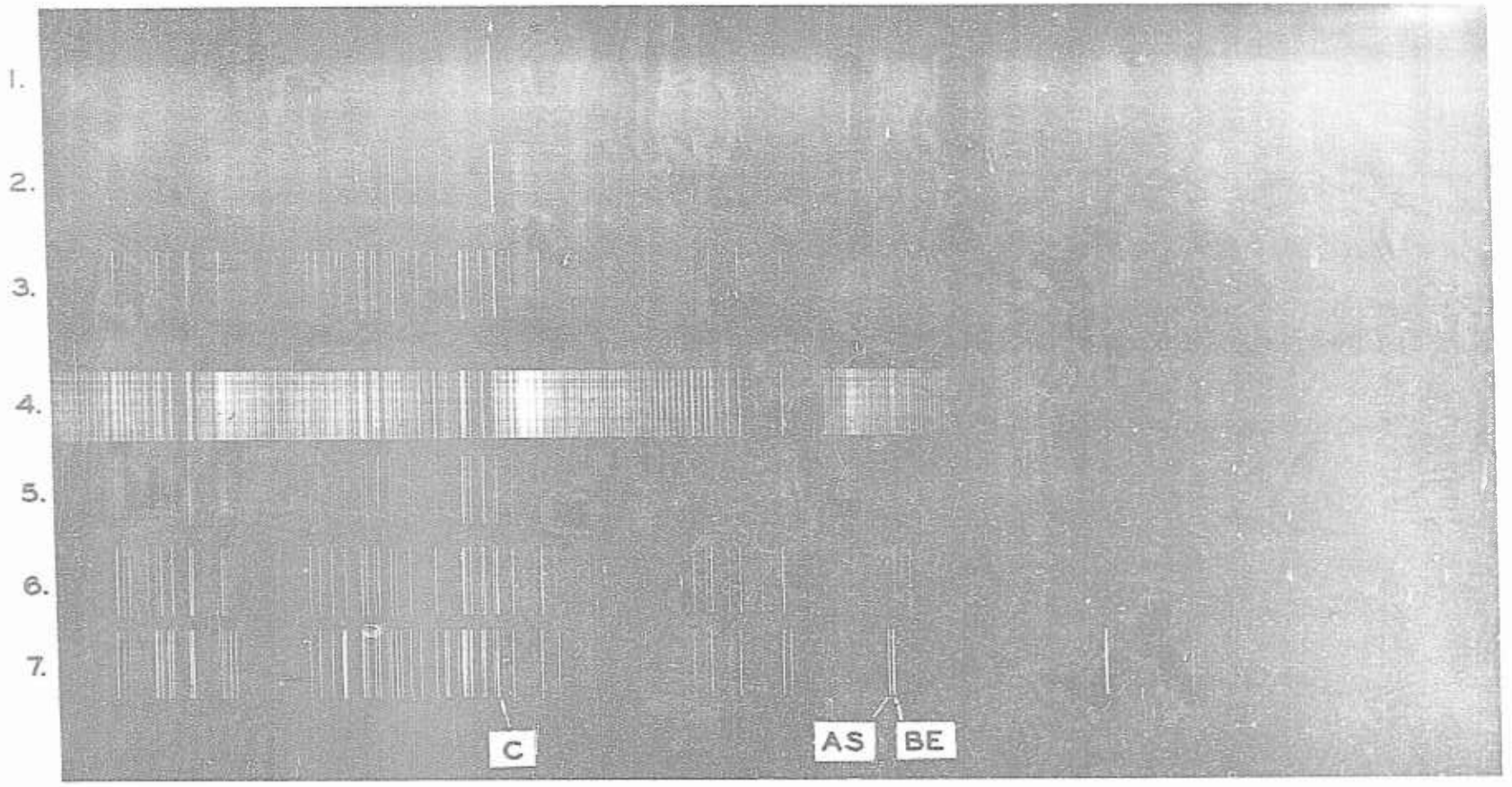

FIGURE 10. SPECTROGRAMS

SPECTRUM NO.

1. BLANK CARBON ELECTRODES
2. 10% BUFFERED FORMALIN
3. LUNG, RIGHT MIDDLE LOBE (20 SECOND EXPOSURE)
4. LUNG, RIGHT MIDDLE LOBE (25 SECOND EXPOSURE)
5. LYMPH NODE, RIGHT HILAR
6. R.U. POWDER (1:5 CARBON DILUTION)
7. R.U. POWDER, UNALTERED

C= CARBON; AS= ARSENIC;
BE = BERYLLIUM

per millimeter and is therefore sufficient to resolve the beryllium line from any interference. The exception to element interference is due to background, or the line caused by the carbon arcing, which is not a true line. On this plate the background is pronounced but is not sufficient to cause the density at the site of the beryllium line seen in spectrum 3 and 4. This is shown by the lack of density in the background of the spectra preceding and following. No evidence of beryllium was present in a second spectrographic examination of tissue from the right middle lobe of the lung nor in tissue from a lymph node in the hilum of the right lung.

2. Analysis for Silicon (WRAMC)

Paraffin block sections of tissue from the right lung were examined for silica or silicates by the ash-hydrochloric acid method. Abundant deposits were found in several perivascular and peribronchial foci of the sections, but exact quantitation was not done. Dr. Johnson stated that quantities of this magnitude are seen occasionally in lungs of persons who had no clinical symptoms of pulmonary disease.

3. Analysis for Beryllium and other Elements (FBI)

a. Specimens:

(1) Q1, tissue from right lower lobe
(2) Q2, tissue from left upper lobe
(3) Q3, tissue from left lower lobe
(4) Q4, tissue from lymph node - superior to left bronchus
(5) Q5, tissue from lymph node - calcified right tracheobronchial lymph node
(6) Q6, tissue from liver and pancreas for control
(7) Q7, tissue from right upper lobe
(8) Q8, tissue from right middle lobe, 3 blocks

b. Results:

"Analyses of the seven samples of tissue, Q1 through Q7, failed to reveal the presence of the element beryllium. It was not possible to quantitatively estimate the other metallic elements, due to lack of known standards; however, most of the usual elements found in tissue were present in trace amounts.

"All of the samples were basically similar to one another in the metallic constituents normally found in tissue and all contained aluminum, calcium, sodium and magnesium as major constituents and phosphorus, iron, copper and barium as minor constituents. Specimens Q1 through Q5 and Q7 were similar to one another in trace metallic constituents and differed slightly from the control sample, Q6. The element silicon was slightly higher in specimens Q1 through Q5 and Q7 than in the control specimen Q6. Specimen Q6 on the other hand contained slightly higher percentages of manganese, nickel and chromium than the other specimens and contained traces of cadmium and molybdenum, which two elements were not detected in the other samples.

"A spectrographic examination of the samples of tissue, specimen Q8, failed to reveal the presence of the element beryllium. These samples of tissue were essentially similar in metallic constituents to the samples of lung tissue, Q1 through Q5 and Q7."

4. Normal Chemical Composition of Lung and Liver

A partial list of normal values for various chemicals from the Handbook of Biological Data[37] follows for comparison with results from the tissue analyses from this patient.

"Part II: LUNG

Values are mg/100 gm fresh tissue, unless otherwise indicated

	Component	Man		Component	Man
1	Water, %	78-80	9	Magnesium	7
2	Ash, %	1.1	10	Phosphorus, total	95-120
3	Bromine	0.3-0.7	11	Nucleic acid	250*
4	Calcium	17	12	Potassium	150
5	Chlorine	260	13	Silicon (as total silica)	20-40
6	Chromium, µg/100g	13	14	Sodium	240
7	Copper	0.5-1.4*	15	Zinc	4-15*
8	Iron	2-22	16	Protein, %	14.9-16.7

* dry weight

"Part IX: LIVER

Values are mg/100 gm fresh tissue

	Component	Man		Component	Man
1	Water, %	73-77	11	Lead	0.2
2	Ash, %	1.4	12	Magnesium	17
3	Arsenic	0.15	13	Manganese	0.08
4	Bromine	0.04-0.43	14	Phosphorus, total	180-240
5	Calcium	7.2-9.4	17	Potassium	170-250
6	Chlorine	96-150	18	Silicon	5-20
7	Chromium, µg/100g	0.6	19	Sodium	120-150
8	Copper	1.5-13	20	Zinc	5.4
9	Iron, total	13.4	21	Protein, %	17.0
10	Inorganic	3.0-16.2			

5. Comment

a. Silicon Compounds

The quantity of silica or silicates found in the lungs and tracheobronchial lymph nodes of this patient is not considered unusual for a man with his occupational history. Although focal pulmonary deposits of these compounds may be reduced by demineralization and tissue redistribution, it is not likely that this patient ever had large accumulations of toxic silicates because gross and microscopic examinations of lungs fail to disclose characteristic lesions and he had no history of symptoms suggestive of silicosis.

b. Beryllium Compounds

More than 500 cases of beryllium poisoning had been reported in the United States by 1958[4], and the clinical findings and tissue changes are well documented[5-16]. Analyses for beryllium in tissues from the lungs and tracheobronchial lymph nodes of this patient were requested in an effort to evaluate the possibility that prior exposure to compounds of this element might have caused changes which altered his vulnerability to infection by inhaled B. anthracis organisms.

Beryllium was found by spectrographic examination in a trace amount in one of seven blocks of tissue from the right middle lobe. Beryllium was not detected in tissue samples from other lobes nor in several lymph nodes from the hilar region of the right lung. This element is not a normal component of human tissues.

The results of these spectrographic examinations are not surprising. Gross and microscopic examinations of the lungs disclose no focal granulomatous or diffuse lesions of the types described in detail in man and experimental animals by numerous investigators[5,6,7,8,9,11]. Also, his known exposure to the mineral was limited to brief and intermittent contact with fluorescent light tube phosphors, and all major manufacturers discontinued use of beryllium-containing phosphors in 1949[4]. He had no history of respiratory, dermatological or other clinical symptoms to suggest acute or chronic beryllium intoxication, nor is there a history of such symptoms in his fellow workers at Fort Detrick.

The possibility of a beryllium effect on the lungs is not ruled out by failure to demonstrate the element in any portions of the lungs except for trace amounts in the right middle lobe. Several characteristics of beryllium intoxication make it difficult to determine whether prior exposure to this element might have influenced the pathogenesis of a known infectious disease.

(1) Disparity between magnitude of dose and incidence of disease

Some compounds of beryllium are toxic in minute quantities; definite tissue responses have been produced in animals with beryllium quantities in the order of millimicrograms[14,17]. There is a tremendous difference in

the reactions of individuals to given exposures. Severe or even fatal disease has occurred in some individuals following exposures incredibly small, both as to concentration and as to time of exposure, while other persons with similar or much greater exposures have shown no sign of injury[16].

(2) Disparity between beryllium content of lungs and severity of lesions

Ten cases of chronic beryllium poisoning were discovered in a study of persons residing within 3/4 mile of a plant that produced beryllium compounds[7]. None of these persons had ever been exposed to beryllium occupationally, but all had resided for several years in the vicinity of the plant. Studies of the air at points 3/4 mile from the plant indicated that the beryllium concentration was only 0.01 to 0.1 micrograms per cubic meter. Study of plant operations for the previous eight years disclosed no significant changes in methods of production nor in procedures for exhausting gases and dusts. Autopsy examinations on two of these patients disclosed characteristic lesions of pulmonary berylliosis, but spectrographic analyses of lung tissues showed only 0.93 micrograms per 100 grams of tissue in one patient, and no beryllium could be detected in the other patient. In specimens of lung tissue from two other individuals who died with non-occupational berylliosis, the beryllium content was only 0.24 and 1.6 micrograms per 100 grams of tissue[7,9,10].

(3) Retention and redistribution of different beryllium compounds in tissues

If minute amounts of beryllium compounds were deposited in the tissues of the respiratory system of this patient many years ago, some decrease in quantity could have occurred due to demineralization or redistribution in tissues. The relatively insoluble beryllium compounds, such as the oxide and the silicate, are retained in tissues for longer periods than the more soluble compounds. Chronic beryllium poisoning has been observed only in persons whose exposure has included the relatively insoluble compounds, usually the oxide; many beryllium compounds are known to cause acute beryllium poisoning[16]. In our case the occupational history indicates no known exposure except to the oxides and the silicates in the phosphor material, usually written $ZnBeMg(SiO_4)Mn$.

Dutra and co-workers[12] have shown that experimental animals exposed to aerosols containing beryllium oxide retain the compound in lung tissues in a fairly constant amount for several months after exposure. Appreciable concentrations were present for as long as 582 days, but a considerable decrease in quantity had occurred. Concentrations in organs other than the lungs varied considerably in different animals, but were always much lower than those in the lungs. Redistribution of beryllium oxide from the lungs to other tissues seems to have been almost negligible; if appreciable amounts of beryllium were removed by the blood from the lungs, the mobilized material must have been eliminated promptly. In another paper Dutra[10] showed that even the relatively insoluble compounds are eliminated slowly and can be found in the urine.

Beryllium was found in 24-hour urine specimens from 5 of 14 patients with occupational chronic pulmonary berylliosis; amounts ranged from 0.14 to 1.7 micrograms per liter of urine. Beryllium was present in 24-hour specimens from 3 of 5 persons who had non-occupational chronic pulmonary berylliosis, acquired from contamination of air in the vicinity of a beryllium producing plant; quantities ranged from 0.12 to 1.3 micrograms per liter of urine.

(4) Antigenic properties of beryllium

Studies on beryllium intoxication indicate that two types of reactions to the element may occur: (1) a regular, primarily irritating, straightforward type of occupational chemical intoxication and (2) a modified immunologic response in which beryllium is the specific allergin[16,17,18]. Beryllium may combine with protein to form an antigen, which in turn stimulates a beryllium-specific antibody; inflammation results from the subsequent reaction of beryllium and this specific antibody as the metal is gradually released from the body stores[16]. Sterner and Eisenbud[16] list several manifestations of beryllium intoxication which are inconsistent with the usual concept of straightforward chemical intoxication, but are accounted for by the immunological response to the metal. Prominent among the dissonant factors are:

(a) The marked disparity between the magnitude of the exposure and the incidence of the disease.

(b) Levels of exposure considerably below what would be considered significant for other occupational toxins have caused severe or even fatal disease.

(c) The considerable delay in some cases between the exposure period and the onset of the disease.

(d) The disparate relation at autopsy between the beryllium content of the lung and the severity of the pathologic effects.

The intensity and type of immunological response of tissues to beryllium could alter the rate of its elimination from the body. A point of interest and possible significance in this case is the detection of beryllium only in the right middle lobe. This lobe was the site of the only focal, nodular, hemorrhagic lesion of pulmonary parenchyma, and at approximately this site a radiodensity was present on a routine x-ray film of the chest taken several years prior to the terminal illness.

(5) Other Elements

All samples of lung and mediastinal lymph nodes contained aluminum as a major constituent and barium as a minor constituent. These elements are not normally found in these organs. Liver and pancreas aggregates contained nickel, cadmium and molybdenum, which are not usually present in significant amounts. Clinical and pathological abnormalities in this case are not attributed to these elements. The patient's occupational history probably accounts for their presence.

C. REFERENCES

1. Thorne, C.B., and Belton, F.C.: "An agar diffusion method for titration of B. anthracis immunizing antigen and its application to a study of antigen production," J Gen Microbiol 17:505-516, 1957.

2. Smith, H., and Keppie, J.: "Observations on experimental anthrax: demonstration of a specific lethal factor produced in vivo by B. anthracis," Nature 173:869-870, 1954.

3. Handbook of Biological Data, W. S. Spector, Editor, W. B. Saunders Co., Philadelphia, 1956, pp 71, 74.

4. Schuber, J.: Beryllium and berylliosis," Sc Am, 199:27-33, 1958.

5. VanOrdstrand, H.S., Hughes, R., DeNardi, J.M., and Carmody, M.G.: "Beryllium poisoning," J A M A, 129:1084-1090, 1945.

6. Hardy, H.L., and Tabershaw, I.R.: "Delayed chemical pneumonitis occurring in workers exposed to beryllium compounds," J Indust Hyg & Toxicol, 28:197-211, 1946.

7. Eisenbud, M., Wanta, R.C., Dustan, C., Stedman, L.T., Harris, W.B., and Wolfe, B.S.: "Non-occupational berylliosis," J Indust Hyg & Toxicol, 31:282-294, 1949.

8. Cardner, L.U.: "Generalized pulmonary granulomatosis occurring among workers believed to be exposed to beryllium or its compounds," Health in Industry, Transactions Eleventh Annual Meeting, Industrial Hygiene Foundation of America, Bull No. 8, pp 89-94, 1946.

9. Dutra, F.R.: "The pneumonitis and granulomatosis peculiar to beryllium workers," Am J Clin Path, 24:1137-1164, 1948.

10. Dutra, F.R., Cholak, J., and Hubbard, D.M.: "The value of beryllium determinations in the diagnosis of berylliosis," Am J Clin Path, 19: 229-234, 1949.

11. Dutra, F.R.: Experimental beryllium granulomas of the skin," Arch Indust Hyg & Occup Med, 3:81-89, 1951.

12. Dutra, F.R., Largent, E.J., Cholak, J., Hubbard, D.M., and Rith, J.L.: "Persistence of beryllium oxide in lungs after inhalation of dust," Arch Indust Hyg & Occup Med, 4:65-73, 1951.

13. Aldridge, W.N., Barnes, J.M., and Denz, F.A.: "Biochemical changes in acute beryllium poisoning," British J Exp Med, 31:473-484, 1950.

14. Stokinger, H.E., Sprague, G.F., Hall, R.H., Ashenburg, N.J., Scott, J.K., and Steadman, L.T.: "Acute inhalation toxicity of beryllium," Arch Indust Hyg & Occup Med, 1:379-397, 1950.

15. Schepers, G.W.H., Durkan, T.M., Delahant, A.B., and Creedon, F.T.: "The biological action of inhaled beryllium sulfate," Arch Indust Health, 15:32-54, 1957.

16. Sterner, J.H., and Eisenbud, M.: "Epidemiology of beryllium intoxication," Arch Indust Hyg & Occup Med, 4:123-151, 1951.

17. Schuber, J., and White, M.R.: "Effect of citrate salts and other chemical factors on distribution and excretion of beryllium," J Lab & Clin Med, 35:854-864, 1950.

18. Cash, R., Shapiro, R.I., Levy, S.H., and Hopkins, S.M.: "Chelating agents in the therapy of beryllium poisoning," New Eng J Med, 260: 683-686, 1959.

V. MICROSCOPIC EXAMINATION
(USAMU Pathology Accession No. 332)

A. STAINS

All sections are stained with hematoxylin and eosin (H&E), unless designated specifically as Giemsa, Masson, Gridley reticulum, acid-fast or Brown and Brenn (B&B) stains.

B. INDEX OF TISSUES SELECTED FOR MICROSCOPIC STUDY

1. Respiratory System

Block No.	Tissue
71	Epiglottis; vertical section, mid-line, with adjacent pharynx.
73	Larynx; anterior wall of vestibule, 5.0 mm to right of mid-line.
72	Vocal cord; right, 7.0 mm from mid-line, vertical section.
74	Larynx; vertical section, across tracheal junction, posterolateral wall.
84	Trachea; complete cross section, 3 cm superior to bifurcation.
83	Lung; right apex, apical-posterior segment.
128	Lung; right upper lobe, 5 cm posterolateral from apex, apical segment.
85	Lung; focal, nodular, 1.5 cm, hemorrhagic lesion, mid-anteroinferior margin, right middle lobe, junction lateral and medial segments.
86	Lung; adjacent to block No. 85, laterally.
145	Lung; right middle lobe, region immediately medial and superior to focal hemorrhagic lesion.
146	Lung; right middle lobe, region immediately adjacent to No. 145, toward hilum, along course of major bronchi and vessels to middle lobe (2 blocks).
147	Lung; right middle lobe, 2 cm superior and medial to focal hemorrhagic lesion.
129	Lung; right lower lobe, anterior margin, lateral basal segment.
90	Lung; right lower lobe, inferior margin, anteriorly, anterior basal segment.

82 Lung; left, apex, apical segment.

139 Bronchus; to anterior segment, left upper lobe; adjacent lung and lymph node.

131 Lung; left upper lobe, superior segment, lingular division, 4 cm distal to bifurcation of left main bronchus.

144 Lung; left, inferior lingular division; includes area of pleura with "violin-string" adhesions.

138 Lung; left lower lobe, anterior medial basal segment.

137 Lung; left lower lobe, lateral basal segment.

130 Lung; left lower lobe, 5 cm superior to inferior margin, posterior basal segment.

149 Lung; left lower lobe, posterior basal segment.

2. Lymphatic and Hematopietic Systems

Block No.	Tissue
1	Spleen; sub-capsular cyst.
9	Spleen; sub-capsular hemorrhage (stasis?).
6	Spleen; mid-posterior margin.
10	Spleen; accessory spleen No. 1.
5	Spleen; accessory spleen No. 2.
19	Bone marrow; vertebral (2 blocks).
22	Bone marrow; sternal.
23	Bone marrow; rib.
80	Thymus; substernal soft tissues, 1 cm superior to No. 79.
81	Thymus; substernal soft tissues, 1 cm superior to No. 80.
64	Vein; left inferior thyroid, plexus; thrombus; lymph nodes (See 3. Cardiovascular System).
65	Veins; hemorrhagic soft tissue; lymph node, at inferior pole of thyroid, right (See 3. Cardiovascular System).

66 Parathyroid glands; right; adjacent lymph nodes (See 6. Endocrine System).

69 Lymph nodes; paratracheal, and soft tissue, 1 cm inferior to lower margin of right lobe of thyroid (4 nodes, 2 blocks).

79 Lymph node and mediastinal fatty tissues immediately posterior to sternum; 2 cm superior to highest point of aortic arch.

78 Lymph node; mediastinal situated in soft tissues on pericardium, immediately anterior to bifurcation of pulmonary artery.

49 Lymph node; paratracheal, right, 5 cm superior to bifurcation of trachea and adjacent mediastinal tissues.

76 Lymph node; paratracheal, right, adjacent to anterolateral wall of trachea; this section and No. 77 represent 1/3 of vertical section through large node, 3 cm above bifurcation of trachea.

77 Lymph node; continuation of area of No. 76.

87 Lymph node; vertical section of large node filling space anterior and inferior to bifurcation of trachea.

88 Lymph node; continuation of section No. 87.

43 Lymph node; hilum of left lung, at bifurcation of left main bronchus.

45 Lymph node; hilum of right lung, posterior to bifurcation of right main bronchus.

125 Lymph node; hilum of left lung, inferomedial to bifurcation of left main bronchus, adjacent to pulmonary vein.

126 Lymph node; hilum of left lung, immediately posterior to No. 125.

127 Lymph node; peribronchial, 5 cm distal to bifurcation of trachea, adjacent to right inferior lobe and to right pulmonary vein.

136 Lymph node; adjacent to bronchus to medial segment of right middle lobe; includes wall of right pulmonary artery.

16 Lymph node; adjacent to superior mesenteric artery.

140 Lymph node; between and posterior to bronchi to right upper and middle lobes.

141 Lymph node; between pulmonary artery and right main stem bronchus.

142 Lymph node; anterolateral aspect of trachea at bifurcation, and anterior to bifurcation of right main stem bronchus at branch to upper lobe.

143 Lymph node; at bifurcation of right main stem bronchus into branches for right middle and lower lobes.

3. Cardiovascular System

Block No.	Tissue
91	Pericardium; opposite mid-left ventricle.
92	Heart; apex, right ventricle.
132	Heart; vertical section through aortic valve; extends superiorly to origin of right coronary artery; includes small area of right and left ventricular linings and base of tricuspid valve.
93	Heart; left ventricle, 6 cm superior to apex, includes anterior descending branch of left coronary artery.
133	Heart; region immediately inferior to No. 132; near site of needle puncture wound of heart.
134	Heart; through posterior cusp of mitral valve.
150	Heart; right ventricle, 2 cm superior to apex.
135	Aorta; arch, inferior wall, 2.0 cm distal to origin of left common carotid artery, longitudinal section.
148	Artery; pulmonary, right longitudinal section, starting at origin.
15	Aorta; mid-abdominal, cross section.
40	Artery; mesenteric.

4. Gastrointestinal System

Block No.	Tissue
70	Pharynx; 1.5 cm anterolateral to entrance of larynx.
75	Pharynx; posterolateral to left superior cornu of thyroid cartilage.
62	Esophagus; 2 blocks (1 - long axis; 1 - transverse).
89	Esophagus; at level of bifurcation of trachea.
33	Stomach; cardia.
32	Stomach.
34	Stomach.

46 Stomach; pylorus.

30 Jejunum; transverse section.

31 Jejunum; long axis section.

29 Ileum; transverse section.

20 Intestine.

21 Intestine.

48 Intestine; through focal lesion described grossly.

36 Appendix; mesoappendix, transverse and longitudinal section (2 blocks).

35 Cecum.

58 Rectum; immediately above anus.

24 Liver.

25 Liver.

26 Liver.

37 Gallbladder; site of large stone.

38 Gallbladder; at origin of cystic duct.

27 Pancreas.

28 Pancreas.

5. Genitourinary System

Block No.	Tissue
4	Kidney; cyst, right.
11	Kidney; cyst, right.
12	Kidney; right.
13	Kidney; left.
14	Kidney; left.
59	Bladder; posterior wall.
57	Bladder and seminal vesicle.

50 Prostatic vein; inferior left lateral surface, thrombus.

51 Prostate; transverse section, superior third.

53 Prostate; inferior pole, through nodule in midline, posterior to origin of membranous urethra.

54 Prostate; transverse section, mid-gland.

55 Prostate; transverse section through inferior third; includes calcified nodule on surface of gland.

56 Prostate; left half of No. 55.

61 Seminal vesicle; left.

52 Seminal vesicle; right.

2 Testis; right, lower pole.

7 Epididymis and testis; right.

8 Pampinoform plexus; right.

60 Ductus; at bladder.

3 Testis and epididymis; left.

6. Endocrine System

Block No.	Tissue
17	Adrenal; left (2 blocks).
18	Adrenal; right (2 blocks).
41	Pituitary (2 blocks).
109	Infundibulum (listed under 7. Central Nervous System).
63	Parathyroid glands; left.
66	Parathyroid glands; right; adjacent lymph nodes.
67	Thyroid; nodule, left lobe.
68	Thyroid; mid-right lobe.

7. Central Nervous System

Block No.	Tissue
94	Meninges; dura, midline across sagittal sinus, region of parieto-occipital fissure.
95	Dura; over right parietal lobe.
96	Pineal body and adjacent structures; vertical section.
97	Hippocampal gyrus; region of caudate nucleus, frontal section, left side.
98	Frontal lobe; left, 1 cm from anterior pole, frontal section.
99	Right ofactory bulb and nerve.
100	Third ventricle; mammary bodies and optic tracts; frontal section.
101	Brain; immediately superior to No. 100, midline to left.
102	Occipital lobe; right, frontal section, 1.5 cm from pole of occipital lobe, extending from midline to right.
103	Parietal lobe; left, superior parietal lobule, 2 cm anterior to transoccipital sulcus, frontal section.
104	Frontal lobe; superior frontal gyrus, frontal section, 7 cm posterior to pole of frontal lobe.
105	Temporal lobe; left, across inferior and midtemporal gyri, 3 cm anterior to transoccipital sulcus.
106	Optic tracts; 1 cm posterior to optic chiasm, base of infundibulum, 3rd ventricle.
107	Lateral ventricle; left immediately superior to No. 106 and to left of midline.
108	Internal capsule and putamen, immediately lateral to No. 107.
109	Infundibulum of pituitary; optic nerves at chiasm.
110	Rostrum of corpus callosum; both lateral ventricles, parolfactory area, caudate nuclei; frontal section; level is 1.5 cm anterior to optic chiasm. Block includes anterior cerebral artery.
111	Brain; same level as No. 110, area immediately to left; includes internal and external capsules, caudate nucleus, putamen, and claustrum.

112 Choroid plexus; from posterior horn, right lateral ventricle.

113 Brain; frontal section, 1 cm posterior to level of mammary bodies; base of peduncle, thalamus.

114 Brain; frontal section, same level as No. 113, part of block No. 113, at the same level with margin 5 mm to left, includes tip of hippocampus.

115 Spinal cord; approximately level of second cervical nerve roots.

116 Transition between medulla oblongata and spinal cord; includes vertebral arteries.

117 Medulla oblongata; level of olive.

118 Pons; mid-portion, anterior half of horizontal section.

119 Pons; posterior half of horizontal section, level of No. 118.

120 Pons; horizontal section, level of brachium pontis, right.

121 Pons; horizontal section, level of pontine nuclei; includes fourth ventricle.

122 Pons; part of same horizontal section as No. 121, immediately to left, approximate level of trigeminal nerve root; includes cerebellum.

123 Cerebellum; level of dentate nucleus; horizontal section.

124 Cerebellum; horizontal section, left hemisphere, anterolateral portion.

42 Spinal cord; mid-cervical (2 blocks).

8. Miscellaneous

Block No.	Tissue
39	Skeletal muscle; psoas, right.
44	Clot; exact site unknown, one of mediastinal vessels (2 blocks).

C. DESCRIPTION OF FINDINGS

1. Respiratory System:

a. Larynx: (Blocks - 4; sections - 4) (Figures 11-13) The apex and anterior surface of the epiglottis are covered by intact, stratified, squamous epithelium which extends to the base of the tongue and lines the crypts invaginating tonsillar tissue. On the posterior epiglottic surface there is normal transition to ciliated, pseudostratified, columnar epithelium, which continues downward to form an intact lining of the entire larynx, except for focal areas of squamous epithelium in the regions of the vocal cords and the aryepiglottic folds.

The lamina propria is diffusely edematous, congested, and infiltrated by scattered lymphocytes, plasma cells, histiocytes, and monocytes; neutrophils are seen rarely. These cells are most numerous in the zone immediately beneath the epithelium. In deeper layers of the wall, among glands, muscle, and cartilage, inflammatory cells are sparcely distributed gene-ally in perivascular regions. Many of the plasma cells and monocytes have vacuolated cytoplasm, and many contain irregular, acidophilic granules or bodies reminiscent of Russell bodies. Plasma cells frequently have dense eosinophilic cytoplasm. Small, non-encapsulated and poorly demarcated subepithelial aggregates of lymphocytes without follicles are present occasionally in all regions of the laryngeal mucosa, but are most numerous over the posterior surface of the epiglottis and the aryepiglottic folds. A few, small, focal, mucosal hemorrhages lie in the subepithelial zone over the epiglottis and the laryngeal vestibule; there are numerous, more diffuse mucosal hemorrhages in inferior portions of the laryngeal wall which extend into deeper layers. These regions are more edematous, and are infiltrated by fewer inflammatory cells than more superior portions of the wall. Extravascular erythrocytes are generally well-preserved; focal hemorrhages appear to be recent in origin. Population and structure of tubulo-acinous, mixed mucous glands in indentations of the epiglottic cartilage and elsewhere in the larynx are not remarkable; the ducts of some glands are dilated and filled with mucus. Goblet cells among surface epithelial cells are more numerous and active in the lower portions of the larynx. In the lamina propria, no significant changes are seen in small nerve trunks, which are most numerous over the posterior epiglottic surface.

The epiglottic cartilage is covered by thin intact perichondrium; lightly stained, edematous, loose, fibroelastic tissue elements separate cartilage cells in several foci. The thyroid and cricoid cartilages have the usual scattered foci of calcification; a narrow zone of ossification is present in one subperichondrial region of the thyroid cartilage. Skeletal muscle is included in the section from several regions of the laryngeal wall, the right vocal cord, and from the base of the tongue. Muscle fibers lie in loose, edematous, connective or adipose tissue, and are more widely separated than usual. Individual fibers vary in staining qualities, size, and density of cell interiors. The cytoplasm of many cells is granular and clumped or partially converted to a dense, hyaline, acidophilic material without cross-striation. Most sarcolemmal sheaths and nuclei are not remarkable; a few

are irregular and surround clumps of degenerating muscle and aggregates of granular, brown pigment. Little or no inflammatory response is seen. The changes in striated muscle are most marked near the epiglottic attachment.

The location and nature of the alterations suggest the changes might be secondary to trauma associated with instrumentation of the larynx approximately one year before admission during the difficult examinations and operations for carcinoma of the vocal cord.

A section through the anterior third of the right vocal cord discloses the usual rather abrupt change from laryngeal, ciliated columnar epithelium to intact squamous epithelium. The lamina propria is moderately edematous and congested; it varies moderately in width and in density of connective tissue elements; inflammatory cells are similar to those elsewhere in the larynx, although fewer in number. There are a few, recent, scattered, small subepithelial hemorrhages.

The epithelium over the true vocal cord is irregularly widened by focal regions of moderate acanthosis and dyskeratosis. In the area of most marked change, the epithelium is two to three times normal thickness and is covered by a narrow zone of parakeratotic cells and keratin debris. Epithelial cells extending from the intact basement membrane to this superficial layer are pleomorphic with considerable variation in size, staining qualities, nuclear:cytoplasmic ratios, and in nuclear morphology; the normal architecture is almost completely lost at all levels. Intercellular bridges and spaces are prominent throughout almost the entire width of the epithelium. Most cells have large vesicular nuclei with prominent, central, acidophilic nucleoli, and dense aggregates of basophilic material along the nuclear membranes. A few scattered cells are pyknotic or are larger than normal, with intensely basophilic nuclei and dense, hyaline, acidophilic cytoplasm. Mitotic figures while not numerous, are seen without difficulty at almost all levels of thickened epithelium.

These regions of epithelial change are at or near the site of previous vocal cord surgery. There is no evidence of invasion and the lesion is considered in the category of focal dyskeratosis or atypical hyperplasia. Some pathologists would probably classify this vocal cord lesion as a carcinoma-in-situ.

Several regions of tonsillar tissue and a small segment of pharyngeal mucosa are included in the vertical section of the epiglottis. Aggregates of tonsillar lymphoid tissue form distinct follicles which are delineated by thin fibrous septae from underlying and adjacent loose, connective and adipose tissue, muscles, and glands. A few scattered lymphocytes, plasma cells, monocytes, and a rare neutrophil, lie at various levels among the cells of the intact squamous epithelium. Inflammatory cells are rarely seen in deeper layers of the mucosa or among submucosal structures. The tonsillar tissue consists mainly of adult lymphocytes; several distinctly formed follicles have lightly stained germinal centers, with loosely arranged, widely separated cells. Pleomorphic reticulum cells are widely scattered among other elements; mitoses are rare. Many cells are pyknotic; others have fragmented or vacuolated cytoplasm and indistinct cell margins. Extracellular and phagocytized cell debris

are noted at multiple sites. Plasma cells and histiocytes are numerous in the subepithelial zone and are seen occasionally in deeper regions. Leucocytes of varied types often occupy intraepithelial positions.

b. Trachea: (Blocks - 2; sections - 2) (Figures 14,15) Alterations in the trachea are comparable to those in the larynx but are more advanced, increasing in severity as the trachea descends. Lining epithelium is intact, ciliated and regular at the origin. In the lower third, the basement membrane is intact, but in many areas covering epithelium is edematous, infiltrated by inflammatory cells, and partially or completely lost. The lamina propria is widened by edema, congestion, infiltration by scattered inflammatory cells, and focal hemorrhages, which become almost continuous in lower portions of the trachea. Erythrocytes lying free in mucosa are intact and stain normally. Infiltrating macrophages contain little or no hemosiderin. In several regions of mucosa and peritracheal connective tissues there are early degenerative changes characterized by loss of cell detail and homogeneous eosinophilic staining of ghost-outlines of structures lying in proteinaceous material. No remarkable lesions of tracheal cartilages or tubulo-acinous mixed glands are seen; ducts of some glands are distended with mucus.

c. Lungs:

(1) Right lung: (Blocks - 10) (Figures 16-31) The apex displays changes characteristic of an old primary, tuberculous complex. An irregular subpleural zone of dense fibrous tissue is fairly well demarcated from underlying, relatively normal parenchyma. Isolated in the scarred region are irregular, often dilated alveolar, bronchial, and lymphatic spaces lined by flattened or cuboidal cells. Clumps of pigment-laden macrophages lie in lumina of these spaces and are scattered singly or in aggregates through dense supporting connective tissue, particularly in perivascular lymphatics. Small foci of calcification are associated with some deposits of free or phagocytized brown or black pigment. Many small fragments of pigment material are doubly refractile. Wide areas of the dense fibrous tissue are relatively acellular, but scattered lymphocytes, plasma cells, and histiocytes lie in edematous regions about dilated capillaries in the zone immediately beneath the pleura. Numerous small dilated blood vessels contain intact erythrocytes; one small vein is partially occluded by a rounded organizing thrombus attached along only one margin. Acid-fast organisms are not demonstrated in sections through the center of the lesion.

The pleura is thin and fairly regular except in the apical region and at the site of occasional string-like fibrous adhesions. In a few sites the surface is covered by a single layer of cuboidal mesothelial cells, which are rounded, loosened, and almost detached; stratification is rarely noted. In most areas mesothelial cells cannot be identified, or are flat and form a unicellular surface layer. Inflammatory exudate on pleural surfaces is not seen. The subserous connective tissue layer displays delicate thin fibers separated by edema fluid, dilated capillaries, and infiltrated, scattered lymphocytes, plasma cells, histiocytes, and rare neutrophils. Subpleural lymphatics are almost invariably dilated but contain little or no exudate. Small subpleural lymphoid aggregates are numerous; these show no definite architectural pattern and lack follicular structure. In numerous subpleural foci black or brown-black pigment is heavily deposited in connective tissue, lymphatics, and macrophages.

(a) Right Upper Lobe: (Blocks - 2; sections - 3, 2 H&E, 1 acid-fast) A few fibrous septae extend irregularly for several millimeters from the apical lesion in the right upper lobe into adjacent parenchyma. Small regions of emphysema and one focus of atelectasis are noted in upper portions. Alveoli in other areas have normal structure and are free from exudate and edema fluid, displaying no features of acute or chronic inflammation. There is little evidence of capillary stasis, although small veins and arteries appear slightly dilated. Perivascular regions display varying amounts of free and phagocytized brown and black pigment; dilated lymphatics are seen in the vicinity of most large vessels.

(b) Right Middle Lobe: (Blocks - 7; sections - 14, 8 H&E, 4 Masson, 2 B&B) The most striking finding in the respiratory system is the focal hemorrhagic lesion in the right middle lobe. No comparable lesion is found elsewhere in either lung. Mesothelial cells are indistinct or absent over a thin, intact, slightly irregular and edematous, subserous pleural connective tissue layer. The subpleural zone is intensely edematous, congested, and infiltrated by numerous lymphocytes, monocytes, plasma cells and large phagocytes. A few well-preserved erythrocytes are scattered among leucocytes and widely dilated capillaries. There is an abrupt transition from this zone to the margin of the focal lesion. Its peripheral regions are remarkably uniform in appearance in all areas. A normal alveolar architectural pattern is maintained and is accentuated by widening and an increased cell population of alveolar walls. Alveolar capillaries in walls are distended, engorged with intact erythrocytes and lined by swollen endothelial cells. Septal cells are swollen, loosened, or rounded; many are almost detached and appear ready to enter alveolar lumina. Alveolar walls contain numerous lymphocytes, plasma cells, monocytes and pigment-laden macrophages. Almost every alveolus contains a loosely woven plug of interlacing, coarse fibrin strands. These fibrin masses have contracted and are generally separated from alveolar walls by an irregular clear zone. Fibrin masses are more compact and slightly more basophilic peripherally, accentuating their margins. Bundles of fibrin strands often extend through pores of Kohn into adjacent alveoli. Erythrocytes and a few leucocytes of types seen in alveolar walls are enmeshed in fibrin masses. Many dilated small arteries and veins extend through this zone; none are thrombosed; all are accompanied by dilated lymphatics, which at some points are engorged with lymphocytes. Perivascular regions are infiltrated by tremendous numbers of the cells previously described; brown and black pigment is abundant in clusters of macrophages as well as in supporting stroma. Much of the phagocytized material is doubly refractile. The zone of fibrin-plugged alveoli merges gradually into the central hemorrhagic region of this nodular lesion. All mid-lesion structures are in various stages of degeneration; some alveolar walls are barely discernible and in some lumina it is possible to identify faint outlines of fibrin strands, numerous erythrocytes, infiltrating leucocytes, and pigment-laden macrophages. Architectural landmarks are lost in several completely necrotic foci; an abundance of basophilic granular material and cell debris is scattered throughout. Doubly refractile particles are rarely seen in the center of the lesion. Several small arteries and veins within this central area are occluded by recent thrombi with cellular and fibrinous elements in various phases of degeneration. Walls of these vessels are edematous, infiltrated by inflammatory cells; and, in focal regions, degenerating. A small bronchus within the lesion contains a hemorrhagic, fibrinous

plug in which scattered leucocytes and pigmented macrophages are numerous at the periphery. The columnar epithelium is intact; cilia are present in most areas. Deeper layers of the wall are distorted by edema and infiltrated lymphocytes.

Most alveoli in the edematous zone immediately surrounding the nodular lesion are completely filled with homogeneous, light pink-staining material; hemorrhages and infiltrating leucocytes are few. In the periphery of this zone there is less edema and several small emphysematous regions display large air vacuoles indenting pink proteinaceous material. Numerous very large macrophages occupy most alveoli. These cells have vacuolated cytoplasm and contain pigment and cell debris. A recent subpleural hemorrhage lies lateral to the focal lesion described. Parenchymal tissues only 1.0 to 2.0 cm from the nodular lesion are relatively normal.

(c) Right Lower Lobe: (Blocks - 2; sections - 3) A section through the anterior margin of the lateral basal segment discloses regions of extensive atelectasis alternating with smaller sites of emphysema. Inflammatory cells are rarely seen in alveoli. Phagocytic cells in alveolar walls or free in the lumina contain finely granular brown or black pigment, which is usually doubly refractile. Blood vessels of all sizes are dilated; none are thrombosed. A section through the inferior margin of the anterior basal segment discloses relatively normal lung parenchyma. A recent fibrinous thrombus or embolus occupies a small vein; cellular elements are scant; attachments to walls cannot be demonstrated. A few small emphysematous foci are present. Bronchi in this lobe have intact ciliated epithelium and contain varying amounts of mucus, cellular debris, and occasional erythrocytes. Larger bronchi and arteries invariably are associated with perivascular deposits of brown or black pigment and focal aggregates of lymphocytes.

(2) Left Lung: (Blocks - 8) (Figures 32-35)

(a) Left Upper Lobe: (Blocks - 4; sections - 6, 4 H&E, 1 acid-fast, 1 B&B) The apex of the left upper lobe also shows changes characteristic of an old primary tuberculous complex, and the lesion is fundamentally similar to the one in the right apex although less extensive. Bronchi in this lesion are more numerous, larger, and more dilated than those in the right apex. Ciliated columnar epithelium lines most of these bronchi but in some areas is flattened or absent. The region immediately below the apical scar is comparable to the corresponding site in the right lung. The walls of larger bronchi near the hilum are thickened by diffuse edema and multiple submucosal hemorrhages. Masses of well-preserved erythrocytes often form subepithelial layers and lie among separated smooth muscle bundles, but hemorrhage is rarely seen in bronchial glands or outer layers of the walls. Numerous lymphocytes, plasma cells, monocytes, and large macrophages infiltrate the mucosa diffusely and are scattered in smaller numbers through all layers of the wall. Many dilated lymphatics lie in and about bronchial walls. Ciliated columnar epithelium is intact in most areas but in several rather extensive sites is partially or completely lost with exposure of frayed basement membrane. Mucus-filled goblet cells are numerous in regions of well-preserved epithelium but are rarely seen at sites of degeneration. In one area of the bronchus to the

anterior segment the lining epithelium is devoid of cilia; cells are rounded at the basement membrane and flattened over the surface; many nuclei are hyperchromatic. The appearance is suggestive, but not characteristic, of squamous metaplasia. Clumps of mucoid or fibrinous material with enmeshed erythrocytes, cell debris, and a few inflammatory cells, including pigment-laden macrophages frequently lie on the mucosa. Sections through lower portions of the lobe display alterations fundamentally similar to corresponding regions of right lung. String-like adhesions and pleural irregularities are more numerous on the left and wider areas of pleura on this side are covered by cuboidal cells. In atelectatic regions a few small veins contain recent thrombi or emboli composed mainly of fibrin with a few enmeshed cells; walls of involved vessels are thin and regular; attachments to endothelial surfaces cannot be demonstrated.

(b) Left Lower Lobe: (Blocks - 4; sections - 5, 4 H&E, 1 Masson) Alterations in the left lower lobe are generally comparable in type, severity and extent to those already described in other lobes except the right middle lobe. Atelectasis, edema and congestion are more severe in some regions of the posterior and lateral basal segments. The lung parenchyma in many sites is relatively normal, and in all sections the almost complete lack of participation by neutrophils in the inflammatory process is a striking feature.

Many small arteries in all lobes have thickened walls, and some are occluded by old thrombi or emboli; some are recanalized. Abundant deposits of anthracotic material and probably other pigments and minerals along the courses of bronchi, blood vessels, and lymphatics are a prominent feature throughout all lobes. These regions display increased dense connective tissue and may well impair normal lymph flow.

2. Lymphatic and Hematopoietic Systems

a. Spleen: (Blocks - 5; sections - 7, 5 H&E, 2 B&B) (Figure 36) Capsules of the spleen and both accessory spleens are normal in thickness and structure; infiltrating cells are rare. Mesothelial cells are flattened or low and cuboidal forming a single surface layer. Adipose and loose edematous connective tissues surrounding the two accessory spleens are infiltrated by a few scattered lymphocytes, plasma cells and histiocytes. Blood vessels and nerves in these perisplenic tissues are not remarkable. Dilated thin-walled lymphatics are often seen in perivascular regions.

The unilocular cyst on the midanterior surface lies immediately beneath the thinned capsule and is lined by a single layer of cuboidal cells. The lumen is irregular; a few small papillary projections extend from the surface. There is no true capsule; lining cells lie directly on compressed parenchyma or trabeculae.

Anastomosing fibrous trabeculae extending from the capsule throughout the spleen display no abnormalities. Malpighian corpuscles are inconspicuous, widely separated, irregular, generally smaller than normal, and lacking in germinal centers. Central arterioles are sclerotic; lymphoid tissue is minimal or absent about many arterioles. Hyperplasia of pulp cells and infiltration of

various cell types accounts for most of the increased cell population and for the indistinct sinusoidal outlines. Throughout the white pulp and in sinusoidal lumina are large lymphocytes, monocytes, histiocytes, plasma cells and large macrophages, which generally contain brown or black pigment and cellular debris; erythrophagocytosis is observed in many regions but is not observed as frequently as in mediastinal lymph nodes; it is not considered a major finding in the spleen. Hyperplastic reticulum cells vary widely in appearance; many have large hyperchromatic nuclei with one or more nucleoli; mitoses are rare. Giant cells, generally mononuclear, are noted occasionally in all areas; a few cannot be differentiated with certainty from megakaryocytes; other cells indicating extramedullary hematopoiesis are not seen. Plasma cells vary widely in size, nuclear:cytoplasmic ratio, cytoplasmic staining qualities; a few have two nuclei. Sinusoidal lining cells are swollen, frequently rounded, and almost detached. Neutrophils and eosinophils are seen occasionally. The degree of stasis varies in different areas but is not marked. However, in several sites the sinusoids are engorged with erythrocytes; in a few areas focal hemorrhages are observed, as in the subcapsular area noted grossly. Many phagocytized particles in all areas are doubly refractile. Focal abscesses are not found. Alterations in pulp of accessory spleens are comparable to those described for the major organ.

b. Lymph nodes: (Blocks - 23; sections - 47, 27 H&E, 5 Giemsa, 2 Masson, 4 Gridley, 5 acid-fast, 4 B&B) (Figures 37-48) The lymph nodes show more changes than any other organ of the body. Lymph nodes of the neck and thorax are more extensively involved than those in any other area.

Architectural features of cervical lymph nodes are barely discernible or are lost due to extensive edema, congestion, and diffuse hyperplasia. In a few of the smaller nodes it is possible to detect the outlines of follicles, but they are indistinct and do not have germinal centers. Most of the cervical nodes have thin, intact, fibrous capsules and widely dilated peripheral sinuses. Similar, but generally less marked, dilation of sinuses is noted in nodes which still retain basic architectural features. These dilated sinuses contain numerous monocytes, large histiocytes, and tremendous macrophages with vacuolated cytoplasm and phagocytized debris. Afferent lymphatics through adjacent edematous and congested supporting soft tissues are dilated and contain various inflammatory cells. Several cervical nodes show more advanced changes characterized by frank hemorrhages into the peripheral sinus or into the stroma, loss of demarcation of sinus boundaries, and extensive disruption of normal elements by tremendous numbers of infiltrating plasma cells, monocytes, histiocytes, and a few neutrophils. There is diffuse hyperplasia of reticulum cells; mitotic figures are numerous. Many of these cells have assumed giant proportions and have large vesicular nuclei and prominent basophilic single or multiple nucleoli. Lymphocytes are seen in all phases of phagocytic activity and in all stages of maturity; some have morphological features of blast cells. Several nodes show focal areas of necrosis in which accumulations of cell debris lie in masses of granular eosinophilic material or masses of phagocytic cells.

The most severe lesions are seen in the large mediastinal lymph nodes. Almost all of these nodes are extensively hemorrhagic; areas in which normal architecture can be made out are rare. Recent thrombi are often seen in

supporting, congested and edematous mediastinal tissues; extensive hemorrhages often extend through the supporting tissues between nodes. In many instances the severe inflammatory and hemorrhagic processes extend through the capsule of the node making its boundaries difficult or impossible to determine. Large hemorrhagic areas generally have erythrocytes in various stages of degeneration, a thick network of coarse fibrin strands, numerous large macrophages containing debris and hemosiderin, and often surround small blood vessels or other structures in which only ghost-like outlines of cells can be made out. Erythrophagocytosis is a common finding. In the non-hemorrhagic areas follicular patterns are completely lost and sinusoidal channels cannot be made out. The stroma is edematous and is packed with hyperplastic reticulum and lymphoid cells intermixed with tremendous numbers of infiltrating plasma cells, monocytes, histiocytes and relatively small numbers of neutrophilic cells. Neutrophils are more numerous in areas of degenerating hemorrhage and in focal areas of necrosis, although it is rare to find them as the predominant cell type. Wide areas of some of the larger nodes are completely necrotic. In several sections it is possible to make out multiple lymph nodes in a single large mass. In the numerous large nodes at the tracheal bifurcation, it is common to find extensive involvement of pericapsular supporting tissues and free extension of the edematous and congested inflammatory lesions through the capsules. All nodes in the efferent chains from the lungs contain large amounts of anthracotic pigment. In some nodes this pigment lies in rather dense aggregates in fibrous tissue stroma, but in others it is more diffusely scattered and in smaller amounts throughout an entire node. Occasional small foci of calcification are detected in the most densely pigmented regions. The large node in the region of the right bronchus which displays the most advanced calcification contains a central mass of amorphous eosinophilic material and fragmented bits of calcium debris with a surrounding dense fibrous zone. No granulomatous foci, acute abscesses, or giant cells are evident.

Bronchial and bronchopulmonary nodes often lie in proximity to primary or secondary bronchi; their capsules are generally intact, but in a few instances there is evidence of the inflammatory process extending through the capsule of the node and into the outer layers of the bronchial walls.

Several sections of the larger nodes showing the most advanced lesions are stained with Brown & Brenn stain for bacteria. Structures having morphological characteristics of B. anthracis are found in foci of necrosis in the large node immediately above the right bronchus and the large node on the anterior aspect of the tracheal bifurcation. These organisms are not doubly refractive contrasting with the formalin and anthracotic pigment deposits.

Abdominal lymph nodes at various sites display congestion, hyperplasia, dilation of sinuses, particularly the peripheral sinus, infiltration by plasma cells, large monocytes, and histiocytes, but do not show the hemorrhage and necrosis which characterized the lymph node lesions in the thorax.

c. Bone Marrow: (Blocks - 4; sections - 8, 4 H&E, 4 Giemsa) Active bone marrow is uniformly distributed through adult-type fat in most sections of two vertebrae, sternum and rib. The fat:marrow ratio is slightly increased. Cellular elements are estimated to occupy 50 to 60 per cent of marrow space in vertebrae and 35 to 45 per cent, in sternum. Bony trabeculae extend normally

from intact cortices, anastomose and radiate in the usual fashion throughout the marrow cavity. Megakaryocytes are normally distributed, but in some places appear slightly more numerous than usual. Most of these cells have abundant, eosinophilic, finely granular or striated cytoplasm and small, darkly stained, irregular, single or multiple nuclei. Cell margins are irregular, indistinct and frayed. A few megakaryocytes have large, vesicular, and folded or shelving, nuclei with prominent basophilic nucleoli; mitoses are not seen. The myeloid:erythroid ratio is slightly increased, being approximately 5 or 6:1, due mainly to an increase in granulocytes in more mature phases of development. Myeloid cells in all stages of development are identified without difficulty. Cells of the eosinophilic and basophilic series are present in normal numbers. Appearance and distribution of erythroid cells is normal. Mitoses of cells in the myeloid and erythroid series are seen occasionally but are not remarkable. All bone marrow sections show moderate diffuse congestion. Most capillaries and sinuses are dilated, filled with intact erythrocytes, and lined by plump endothelial cells. Scattered lymphocytes are found without difficulty throughout the marrow; in every section there are several aggregates of lymphoid cells, the largest occupying one-half to one-third of a high power field. These cells are almost all small, normal, adult lymphocytes. Small numbers of plasma cells, monocytes, large reticulum or histiocytic cells and a few large macrophages with vacuolated cytoplasm are seen associated with lymphoid aggregates and occasionally elsewhere in the marrow. Hemosiderin or other pigment is rarely seen within phagocytic cells or free in the marrow. No focal abscesses, areas of infarction, or infiltrates of acute inflammatory cells are identified. No thrombosed vessels are seen.

d. Thymus: (Blocks - 2; sections - 2) Scattered remnants of atropic thymus lie in widely separated foci in edematous and congested soft tissues of the anterior mediastinum. Some small stellate foci are connected by long narrow columns of lymphocytes extending among lobules of normal fat. Thymic tissue consists almost entirely of aggregates of small adult lymphocytes; mitoses are rare. Epithelial elements are scant and are limited almost entirely to peripheral concentrically arranged Hassall's corpuscles. Most of these corpuscles have calcified centers. A few plasma cells, monocytes and large histiocytes are scattered among the thymic cells.

3. Cardiovascular System: (11 Blocks)

a. Pericardium: (Blocks - 1; sections - 2, 1 H&E, 1 Giemsa) The pleural surface of the pericardium is covered in most areas by a single layer of loosened, swollen, rounded or cuboidal, mesothelial cells. The underlying thin layer of delicate connective tissue fibers is devoid of covering cells in some areas and lies on a layer of normal fat. Recent small focal hemorrhages may be secondary to the needle puncture wound. Mesothelial cells covering the parietal surface form a single layer and are quite similar in appearance to those on the opposite surface; many of these cells have vacuolated, granular cytoplasm and are almost completely detached from the thin surface layer of supporting connective tissue. Deeper in the wall several broad, branching strands of dense hyaline tissue extend through the fat. Small blood vessels are dilated. About many capillaries and in the zones beneath both mesothelial surfaces are scattered plasma cells, lymphocytes, monocytes and a few large phagocytic cells. A few cells have features of mast cells. Neutrophils are rare. Numerous small nerve trunks are not remarkable.

b. Heart: (Blocks - 6; sections - 8, 6 H&E, 1 Giemsa, 1 Masson) The epicardium in most areas is covered by a single layer of swollen, loosened, round or cuboidal, mesothelial cells which at some sites have been lost. The thin layer of connective tissue and elastic fibers is edematous and infiltrated by scattered monocytes, lymphocytes, plasma cells and histiocytes. These cells are more numerous about dilated capillaries and small veins. A small nodule formed by a dense aggregate of lymphocytes lies immediately beneath the epicardial surface over the anterior descending branch of the left coronary artery; smaller collections of lymphocytes are present at other sites. Walls of arteries and veins are rarely penetrated by perivascular infiltrating cells; an exception is a superficial vein in the epicardium of the right ventricle near its apex; here lymphocytes, monocytes and a few neutrophils extend through all layers of the vessel wall in the focal region nearest the surface. In the deeper fatty epicardial zone dilated lymphatics are often seen in the vicinity of larger blood vessels. Abnormalities are not seen in the numerous small nerves or in the fatty tissue.

The endocardium is intact and regular; in most areas a single layer of flat endothelial cells can be identified. In a few regions near apices of both ventricles there is a slight increase in subendothelial connective tissue. A few scattered lymphocytes and monocytes are noted in widely separated regions.

The myocardium is moderately edematous and congested. Muscle fibers are loosened and more widely separated than normal. Muscle cells are well developed and have distinct cross striations. Most nuclear poles contain abundant lipochrome. There is uniformity of cytoplasmic staining and density except for several subendothelial regions in the apices of both ventricles. Myocardial cells in these sites are swollen, rounded, vacuolated and lightly stained. A few lymphocytes, monocytes, plasma cells and histiocytes are present about some dilated capillaries and small veins in the loose supporting connective tissue between muscle bundles. Areas of myocardial infarction or fibrosis are not found. Nerve trunks within the myocardium are not remarkable. A few dilated lymphatics are seen in the vicinity of larger blood vessels.

Major branches of coronary arteries display slight intimal thickening and irregularity due to increased fibrous tissue, accumulation of vacuolated cells, and fraying of elastic fibers. Coronary veins and smaller branches of arteries are not remarkable, except at a few sites of involvement by infiltrating leucocytes. No thrombi or emboli are found.

Valve cusps are moderately thickened. Sections taken through the thickest portions of aortic, mitral and tricuspid valves disclose slight surface irregularities, deposition of fine pigment granules in swollen endothelial cells, and a few infiltrated leucocytes in the subendothelial zone. Supporting dense connective tissue fibers are increased and extend into wide regions of loose, lightly stained chondroid tissue. Dense relatively acellular hyaline tissue in the region of the annulus fibrosus forms a broad irregular zone which extends into the base of the aortic cusps and the origin of the aorta. A few irregular subendothelial regions are occupied by eosinophilic, non-cellular ground substance. No thrombi, vegetative lesions, or focal abscesses are seen.

c. Aorta and Peripheral Vessels: (Blocks - 4; sections - 5, 4 H&E, 1 Masson) Near its origin the aorta displays intimal widening due to an increase in connective tissue elements, accumulation of lipid material in large vacuolated cells, fraying of elastic fibers and infiltration of the edematous subendothelial zone by scattered leucocytes. The internal, elastic lamina is indistinct in some areas due to splitting of fibers and distortion by intimal changes. Between elastic fibers forming the usual network through the media are large vacuolated cells with indistinct margins. In the arch and abdominal portions of aorta these changes are more advanced. Lipid deposits in the intima are larger, more numerous, and often include small foci of calcification; cholesterol clefts occur in many regions. Degenerative changes are more marked in the media and many of the large vacuolated cells contain calcium salts in the form of minute granules. Inflammatory cells are rarely seen within the media. A few plasma cells, lymphocytes, and monocytes lie about dilated lymphatics and vasa vasorum in the edematous adventitia.

Sections of large muscular arteries display slight atherosclerosis with associated variations in intimal width. Muscle layers are relatively normal. Endothelial surfaces are intact; no thrombi or emboli are seen. Arteries supplying individual organs are described elsewhere.

There is generalized venous stasis. Veins in the thorax and neck are often involved in the inflammatory processes of the lymphatic and respiratory systems. Large veins in close proximity to severely involved lymph nodes are frequently infiltrated by inflammatory cells but thromboses are not seen in major vessels. Numerous smaller veins in the neck, mediastinum and lungs contain recent thrombi in various stages of early organization.

4. Gastrointestinal System: (Blocks - 19)

a. Pharynx: (Blocks - 2; section - 2) (Figures 51-54) The pharyngeal wall immediately anterior to the epiglottis was described under 1. Respiratory System. A section through the lateral portion of the oral pharynx includes hyperplastic tonsillar tissue about several deep crypts. Squamous epithelium is intact in all areas; in deeper portions of crypts the epithelium is penetrated by numerous dilated capillaries and infiltrated lymphocytes, plasma cells, monocytes, and neutrophils. Crypts contain keratin masses and other cellular debris. Nodular lymphoid aggregates in the zone beneath the surface epithelium and about the crypts are sharply demarcated by a fibrous capsule. Lightly stained germinal centers of most follicles contain many large vesicular cells and are infiltrated by a few plasma cells, neutrophils, and monocytes. Phagocytized cell debris is usually present. Dilated capillaries are prominent throughout the lymphoid tissues. Numerous mucous glands lie in loose, slightly-edematous connective tissue and among striated muscle fibers in deeper layers of the wall. Normal excretory ducts extend normally to the surface. Intact squamous epithelium covers the pharyngeal surface near the origin of the esophagus. Scattered lymphocytes, plasma cells, and monocytes infiltrate superficial portions of loose submucosa; aggregates of lymphoid tissue are absent. Deeper submucosal zones are occupied by a plexus of thin-walled, dilated veins; none are thrombosed. A few mucous glands lie in the wide layer of loosely-arranged striated muscle fibers in deeper layers of the wall. Inflammatory cells are rarely seen in muscular and glandular regions. No focal abscesses are found in any portion of the pharyngeal wall.

b. Esophagus: (Blocks - 3; sections - 7, 3 H&E, 2 Giemsa, 2 B&B) (Figures 51, 52) Squamous epithelium lining the second quarter of the esophagus is eroded in several areas and is entirely lost in most of the lower half. Numerous neutrophils, lymphocytes, plasma cells, histiocytes, and debris-laden macrophages infiltrate mucosa and submucosa at all levels. Smaller numbers of these cells lie in loose, supporting connective tissue of edematous tunicae muscularis and in adventitia. Plexuses of widely dilated capillaries and veins are prominent in lamina propria and deep in submucosa. In the subepithelial zone many capillaries and lymphatics contain clumps of inflammatory cells similar to those in surrounding tissues. Aggregates of lymphoid tissue are found in the vicinity of some mucous glands or their ducts. Small foci of necrosis are seen in the upper portion of the esophagus. Wide areas of mucosal degeneration in the lower third result in a shaggy lining of degenerating inflammatory cells, epithelial debris, and eosinophilic non-cellular material. At the level of the tracheal bifurcation, cell details of mucosal structures are often lost; blood vessel walls are in various stages of degeneration and focal hemorrhages are present in most edematous regions. Small nerve trunks and sympathetic ganglia in muscularis are relatively unaffected. There is the usual transition from skeletal to non-striated muscle. Muscular coats are edematous but intact in the upper portions; at the level of the tracheal bifurcation, edematous connective tissue with inflammatory cells have pushed muscle bundles widely apart.

c. Stomach and Duodenum: (Blocks - 5; sections - 5) Changes are minimal in the fundus. Superficial epithelium is autolyzed but the mucosa is intact and parietal cells are normal in appearance and distribution. Lymphocytes, plasma cells, and a few eosinophils are scattered in lamina propria; a few lymphoid aggregates lie in the vicinity of intact and regular muscularis mucosae. The muscularis externa is normally formed and is rarely infiltrated by inflammatory cells. Auerbach's and Meissner's plexuses blood and lymphatic vessels are not remarkable.

A section of cardia includes the termination of the esophagus which displays the extensive inflammatory changes already described. The stomach wall is more edematous and congested than is fundus; infiltrating cells are much more numerous; a few are present deep into muscularis mucosae. The usual compound tubular glands are present, and gastric pits have a few parietal cells.

Sections through pylorus and duodenum display a normal sphincter. Pyloric and Brunner's glands are normally formed and distributed in intact mucosa. Lymphocytic infiltration of lamina propria in these regions is more marked than in that of the stomach. Several large aggregates of lymphoid tissue have well developed follicles. Smaller numbers of plasma cells, monocytes, and histiocytes are scattered among lymphocytes. Cells infiltrating deep into muscularis mucosae are rare.

d. Jejunum, Ileum and Large Intestine: (Blocks - 9; sections - 12, 11 H&E, 1 B&B) (Figure 53) The principal lesion in the intestines is a focal region in the jejunum, 140 cm distal to the duodenum. All layers of the wall are extremely edematous, congested, and infiltrated by tremendous numbers of neutrophils, lymphocytes, plasma cells, monocytes, histiocytes and a few eosinophils. Among them are numerous large macrophages containing erythrocytes

and leucocytes in various stages of degeneration. Extravasated erythrocytes, loose fibrinous networks, and eosinophilic non-cellular debris separate degenerating bundles of the muscularis, ganglia and nerve trunks, and elements of supporting stroma. Many dilated capillaries, lymphatics, and small veins contain intact leucocytes and erythrocytes; others contain recent thrombi rich in fibrin; some vessels are degenerating and cell detail is almost completely lost. Surface epithelium is completely lost. Structures thoughout mucosa and submucosa are degenerating and appear only as eosinophilic ghost outlines. An attached segment of mesentery is edematous but displays intact fat, very few inflammatory cells, and relatively normal arteries and veins containing well-preserved erythrocytes. Clumps of intestinal contents on the mucosal surface contain many bacteria; some are cocci; others, bacilli of varied sizes and shapes. None has the morphology of B. anthracis.

Sections of ileum, colon, cecum, rectum and other areas of jejunum exhibit less severe changes of approximately similar nature. Lymphocytes and smaller numbers of plasma cells and monocytes are scattered throughout the slightly edematous lamina propria. Solitary lymphatic follicles and Peyer's patches have normal appearance and distribution. Small numbers of eosinophils are present in all regions, being most numerous in the proximal jejunum. Valves of Kerkring, mucosal villi and intestinal glands are normally formed. Epithelium lining the crypts of Lieberkühn has a normal ratio of columnar to goblet cells; Paneth cells are barely discernible in the proximal jejunum but are prominent in terminal portions. Epithelium over the tips of villi is badly autolyzed in almost all areas, although well-preserved surface cells are seen in the colon. Inflammatory cells are rare in portions of wall deep to muscularis mucosae. Muscular coats display no significant changes. Plexuses of Auerbach and Meissner are not remarkable. Portions of attached mesentery have normal fat content, a few perivascular inflammatory cells, and are only slightly congested and edematous. No thrombi are seen in mesenteric vessels nor in dilated veins of hemorrhoidal plexuses. Lumen of the appendix near its tip is occluded by sheets of dense fibrous tissue and fat which replace mucosa and extend into distorted and fibrosed remnants of muscular coats. Clumps of intestinal contents found adherent to mucosa in various areas are not remarkable. Parasites and ova are not found.

d. Liver and Gallbladder: (Blocks - 5; sections - 5) (Figure 54) A single layer of flat mesothelial cells covers the thin, regular, dense fibrous liver capsule. Normal lobular structure is retained in all regions. Diffuse congestion and edema cause the most pronounced changes in the central portions of lobules. Sinusoids in regions of central veins are usually several times normal width and often form irregular cavernous blood spaces in the centers of lobules. There is corresponding narrowing of hepatic cords. Endothelial and Kupffer cells are separated from hepatic cords in many places by a loose reticulum of fine eosinophilic fibers and granular material. Along walls of dilated sinusoids are monocytes, lymphocytes and neutrophils in greater numbers than are seen in blood in larger vessels. Multiple cytoplasmic vacuoles are present in many monocytes. No focal abscesses are observed. Cytoplasmic deposits of granular brown pigment with the appearance of hemosiderin are seen in liver cords throughout lobules, but are most pronounced in central regions; similar pigment is present in many Kupffer cells. Cytoplasmic vacuoles due to fat

globules are present in hepatic cells in all parts of the lobules; vacuoles are larger and more numerous in cells of the central regions. Parenchymal cells in all regions are deficient in glycogen and have granular eosinophilic cytoplasm. Most nuclei vary only slightly in size and appearance. A few cells contain double nuclei; some have exceptionally large vesicular nuclei with prominent margins and one or more dense nucleoli. No significant alterations are found in connective tissue elements, arteries, bile ducts, veins or portal areas, although almost invariably there are numerous infiltrating lymphocytes with smaller numbers of monocytes and plasma cells, neutrophils and eosinophils are rare. At the hilum, numerous nerves, large bile ducts and blood vessels are not remarkable, although a few arterioles in connective tissue display slight intimal hyaline thickening.

Gallbladder mucosa forms the usual branching fold and has intact, moderately autolyzed and flattened epithelial cells except in areas opposite gall stones. A few Rokitansky-Aschoff sinuses penetrate the muscular coat. Small mucous glands in lamina propria near the neck of the gallbladder are not remarkable. Loosely arranged muscle bundles and connective tissue stroma deep to lamina propria are not unusual. At sites opposite gall stones the mucosa is flattened and epithelium is lost; the wall consists mainly of dense hyaline connective tissue. Lymphocytes are scattered throughout all layers of the wall; at a few sites in mucosa and at the junction of muscular and perimuscular layers there are small poorly-defined lymphoid aggregates. Small numbers of monocytes, plasma cells, histiocytes and rare eosinophils are seen among lymphocytes. The peritoneal surface is intact and regular; it lies on a wide layer of connective tissue and fat in which inflammatory cells are rarely seen. Some small arteries and arterioles in perimuscular connective tissue near the origin of the cystic duct exhibit slight sclerotic changes. Numerous nerves are not unusual. Architecture of a small lymph node near the origin of the cystic duct is obscured by diffuse hyperplasia, edema, and congestion. The peripheral sinus is widely dilated. Scattered through the loose stroma are numerous large reticulocytes with vesicular nuclei, monocytes with abundant vacuolated cytoplasm, plasma cells, and large phagocytes containing cell debris. Neutrophils are rare.

e. Pancreas: (Blocks - 2; sections 2) There is normal lobular arrangement of acini of the pancreas. Loose supporting connective tissue and fat are not remarkable. Acinar cells have the usual secretory granules. Islets of Langerhans are normal in appearance and distribution. No abnormalities are seen in blood vessels, nerves, or pancreatic ducts. Inflammatory cells are absent in most regions; a few lymphocytes are present in occasional perivascular connective tissues.

5. Genitourinary System

a. Kidneys: (Blocks - 5; sections - 5) (Figures 55,56) A large cyst in the right kidney is lined by a single layer of flattened cells; dense relatively acellular, fibrous tissue with parallel hyaline fibers form a zone of varying width immediately beneath the surface. Connective tissue of deeper layers of the cyst wall is looser and encloses many dilated capillaries, scattered lymphocytes, monocytes, plasma cells and histiocytes. Occasionally the cyst lining is separated from relatively normal parenchyma by only a few fibrous strands, but in most regions compressed and degenerating tubules lie

in deeper layers of connective tissue, and there is a gradual transition to functional renal parenchyma.

Except for this large cyst, the kidneys display comparable changes and may be described together. Fibrous capsules are regular, vary only slightly in width, and are infiltrated by few inflammatory cells. Pericapsular edematous fatty and connective tissues are infiltrated by scattered inflammatory cells and permeated by many dilated blood vessels and a few lymphatics. Small irregularly round cysts are numerous immediately beneath the capsule, and occasionally lie deeper in cortex; lining cells are flattened or cuboidal; lumina contain varying amounts of granular eosinophilic or light tan-brown debris. At widely separated subcapsular sites there are a few irregularly triangular small regions of fibrosis; some of these are infiltrated by numerous lymphocytes and a few monocytes and plasma cells. Fibrosis elsewhere in the cortex is rare and limited to small irregular foci involving only a few tubules and glomeruli.

Glomeruli are normally distributed and generally have normal cellularity, although occasionally they are undergoing fibrosis; associated inflammatory processes are not evident; sclerosis is observed at all stages. Capillaries in most glomerular tufts are dilated; widened loops contain intact erythrocytes. At many points there is some narrowing of capillary lumina by foci of slightly basophilic, finely fibrillar or granular material which may represent widening of the basement membrane or accumulation of fibrinoid material in the vessels, or a combination of these processes. These changes appear more pronounced than basement membrane alterations generally associated with formalin fixation. Most Bowman's capsules are thin and regular; a few are slightly thickened. Glomerular spaces are usually empty but some contain small clumps of granular, eosinophilic, proteinaceous material; presence of leucocytes, erythrocytes or debris is rare. No abnormalities are seen in the juxtaglomerular apparatus or openings into convoluted tubules.

Proximal convoluted tubules have normal arrangement and distribution. Lining epithelial cells display slight degenerative changes but many have intact brush-borders and display only slightly increased granularity of cytoplasm. Upper portions of some cells have sloughed off and appear as eosinophilic granular material in the lumina. Other cells contain fine granules of light-brown pigment. Loops of Henle are intact and normally arranged. Variations in lining cells are slight and most of these tubules appear perfectly normal. Eosinophilic hyaline casts or aggregates of granular tan material fill occasional lumina. Granules of yellow-brown pigment are in cytoplasm of a few lining cells. Distal convoluted tubules and collecting tubules are occasionally occluded by casts similar to those in loops of Henle. Epithelial cells display slight degenerative changes and many have cytoplasmic deposits of golden-brown pigment. In a few segments of tubules, mainly in distal portions of nephrons, lining epithelial cells have undergone more advanced degeneration, have often lost nuclei, and exist only as flattened cytoplasmic material covering intact basement membrane. In focal regions of papillae and deeper zones of medulla there are sites of increased stromal connective tissue sometimes containing a few chronic inflammatory cells and small accumulations of calcified material.

Renal pelves are lined by normal transitional epithelium. Supporting fatty and connective tissues are slightly edematous, congested, and infiltrated by scattered lymphocytes, monocytes, plasma cells and a few phagocytes. Subepithelial capillaries are widely dilated; a few small recent hemorrhages are found. Small nerve trunks are not remarkable.

Major branches of renal arteries display minimal arteriosclerosis. Most arcuate arteries are normal; a few show slight intimal widening and irregularity. Almost all afferent and efferent glomerular arterioles are normal; a few of the former are narrowed by widened hyalinized walls; in some, a dense hyaline plaque appears in only one portion of the wall. Capillaries extending among tubules display varied degrees of dilation. In those exhibiting most extreme stasis there are many large lymphocytes and monocytes among intact erythrocytes, particularly along endothelial surfaces. No thrombi or emboli are demonstrated in vessels of either kidney.

b. Ureters: (Included in block with bladder) Transitional epithelium of ureters is a normal continuation of renal pelvic epithelium. Muscular coats of the ureter are not remarkable. Inflammatory infiltrates are not seen.

c. Bladder: (Blocks - 2; sections - 2) Mesothelial cells form a single layer over the peritoneal bladder surface; absence of mesothelial cells in some areas is considered due to handling. Fat and loose connective tissues of the adventitial coat are slightly edematous and congested. Small numbers of lymphocytes, plasma cells and monocytes are found generally in the vicinity of dilated small blood vessels. Several arteries exhibit minimal sclerotic intimal thickening. One small artery contains an organized and partially recanalized thrombus. Numerous small nerve trunks in all regions and several ganglia near the trigone are not remarkable. The muscular layer is not unusual except for slight loosening and separation of fibers. Loose connective and elastic tissue of lamina propria is infiltrated by a few scattered inflammatory cells. In the subepithelial zone of the trigonal region there are numerous tremendously dilated capillaries. Mucosal hemorrhages are not found. Transitional surface epithelium is 1 to 3 cells thick in most areas, but in some cases cannot be demonstrated. In most areas there is no inflammatory response and the loss is probably due to postmortem handling. At a few sites without covering epithelium the surface is irregular and shaggy with projecting strands and clumps of eosinophilic granular material and cell debris.

d. Urethra: (Same block with prostate) Several sections of prostate include segments of urethral wall. In most areas intact transitional epithelium lies on a highly vascular and congested lamina propria. Any loss of epithelium is not associated with inflammatory changes and is probably due to postmortem handling. The subepithelial zone is infiltrated by a few scattered lymphocytes. Openings of prostatic ducts are not remarkable.

e. Testes, Epididymes, Spermatic Ducts, and Seminal Vesicles: (Blocks - 7; sections - 8) The tunica albuginea enclosing each testis is covered by a single layer of flattened mesothelial cells; dense fibrous walls are of uniform thickness. Small blood vessels and nerves are not remarkable. Some perivascular regions are infiltrated by a few lymphocytes. Seminiferous tubules are more widely separated than normal. Supporting stroma is scant, loose, and edematous.

A few lightly pigmented interstitial cells are uniformly scattered throughout the testes; small nests are occasionally seen, generally in the vicinity of dilated small blood vessels. Inflammatory cells are rarely noted. Basement membranes of most seminiferous tubules exhibit fibrous thickening; there is retardation of spermatogenesis. Sperm cells in all stages of development can be found, but mature spermia are present only occasionally. Lumina of most tubules contain small amounts of granular eosinophilic debris; and considerable increases in the ratio of Sentoli cells to spermatogenic elements. In a few tubules all cells are degenerating and have assumed an almost homogeneous eosinophilic staining quality, although cell outlines can still be distinguished. Tubuli recti have usual columnar lining cells and pass normally into the rete testis, whose cavernous spaces are lined by flattened or low cuboidal epithelium; they are empty or contain relatively small numbers of sperm cells mixed with eosinophilic amorphous material and cellular debris. At a few sites spermatids form dense masses in various stages of degeneration and calcification. Ducts of both epididymes are lined by intact typical epithelium and most lumina contain packed masses of sperm cells with very little debris. In one region of the right epididymis the duct lumen contains non-cellular, eosinophilic, hyaline or granular material with no sperm cells. Several clumps appear to lie free in connective tissue stroma; there is no associated inflammatory response. Epididymal stroma is edematous, congested, and infiltrated by scattered lymphocytes, plasma cells, monocytes and a few macrophages. The ductus deferens displays no remarkable changes in a section near its origin; the lumen contains a small amount of debris and a few adult spermatids. The ductus also has normal structure and contains adult spermatids in its terminal portion. No abnormalities are seen in the colliculus seminalis. Multiple sections fail to disclose thrombi in the cavernous venous and capillary blood spaces about the rete testis, epididymis and origin of the spermatic cord. Arterial plexuses are characterized by tortuous vessels having patent lumina containing intact erythrocytes; occasional vessels display slight arteriosclerosis. A section of spermatic cord near its origin exhibits loose stroma and several large bundles of edematous cremasteric muscle with loosened widely separated fibers that vary in staining qualities. Numerous small nerve trunks are not remarkable.

Irregular cystic spaces of seminal vesicles are separated by the usual branching and anastomosing partitions. Most areas are lined by a single layer of cuboidal cells with cytoplasmic vacuoles and large amounts of yellow-brown pigment. Some areas are covered by taller or stratified cells. Lumina contain a lacy reticulum and clumps of non-cellular eosinophilic material. No abnormalities are seen in smooth muscle of walls nor in multiple small sympathetic ganglia and nerves. In a few focal areas the lining epithelium and underlying muscle are degenerated, leaving homogeneous eosinophilic fibers surrounding irregular spaces containing a few round acidophilic concretions. Connective tissue stroma is edematous, congested, and infiltrated by scattered inflammatory cells.

f. Prostate: (Blocks - 6; sections - 6) There is moderate hyperplasia of the prostate; acini display wide variation. Most glandular substance has branching papillary projections covered by tall, columnar, mucus-secreting cells; dilated acini often are lined by flattened or cuboidal cells. Occasional nests of atrophic glands are devoid of epithelium and lie in dense connective tissue. Most acini contain dense round eosinophilic or brown concretions and varying amounts of cell debris. In multiple foci, particularly near the urethra,

periglandular stroma is infiltrated by many lymphocytes. No evidence of malignancy is found. In most regions the fibromuscular stroma is not unusual; many regions are largely fibrous; others display ill-defined bundles of smooth muscle. Some capsular arteries display minimal intimal sclerosis. Venous plexuses are generally normal, but old hyalinized or partially organized thrombi are seen in veins on the posterior surface of the gland; one recent thrombus is found. Pericapsular nerves and sympathetic ganglia are not remarkable.

6. Endocrine System

a. Pituitary Gland: (Blocks - 2; sections - 2) The dense collagenous capsule of the pituitary gland is regular and of normal thickness. Epithelial cells are normally arranged in cords and nests between thin-walled blood-filled sinuses. Acidophilic, basophilic and chromophobic cells are intermixed throughout the anterior lobe in normal numerical proportions. Acidophils predominate and generally have multiple, indistinct, small, cytoplasmic, lipid vacuoles near the nucleus. Much larger single or multiple vacuoles are seen in many basophils. In the denser and less vascular connective tissue stroma of the intermediate lobe are multiple cystic spaces containing homogeneous eosinophilic colloidal material. These cysts vary widely in size, and are lined by a single row of flattened or cuboidal cells. The largest cyst is very irregular and has a single layer of ciliated cuboidal or columnar cells; no colloid is present. A few epithelial cells lie in stroma between cysts. Loose neuroglial tissue of the posterior lobe and infundibulum is not remarkable. Scattered through these regions are large "pituicytes" with abundant cytoplasmic pigment granules. No inflammatory infiltrates, focal abscesses, hemorrhages or thrombosed vessels are seen.

b. Parathyroid Glands: (Blocks - 2; sections - 2) Both right and left parathyroid glands have thin connective tissue capsules from which delicate anastomosing septae extend inward to support numerous wide capillaries, abundant interstitial fat, and endocrine cells. Parenchymal cells are arranged in solid nests, anastomosing columns and small stellate islands. Oxyphilous cells found only occasionally among numerous principal (chief) cells in left glands are numerous in the right glands; at several sites they form solid masses among the numerous principal cells. No cysts or true glandular arrangement of parenchymal cells are noted. There is no evidence of inflammatory changes nor of vascular lesions. Several small lymph nodes close to the right parathyroid display dilation of the peripheral sinus, diffuse edema, congestion, and hyperplasia. Aggregates of large phagocytes in the subcapsular zone contain large amounts of hemosiderin. No abscesses are seen; neutrophils are rare among numerous plasma cells, monocytes, and histiocytes.

c. Thyroid Gland: (Blocks - 2; sections - 2) The thin loosely arranged connective tissue capsule of the thyroid is continuous, with dense fibrous strands extending through the gland and dividing it into the usual lobes. In many regions these septae are composed of compactly arranged, broad collagen fibers; some sites are relatively acellular and hyaline. Acini vary widely in size, but are generally small, and lined by single layers of low cuboidal or flattened epithelium; almost all contain homogeneous, lightly eosinophilic colloid without peripheral vacuolation. Colloid in a very few acini is broken up into globular masses or appears as dense homogeneous basophilic material.

Colloid-appearing material lies free in stroma in a few sites. No lymphoid aggregates are found; inflammatory cells are rare. No significant changes are seen in blood vessels or nerves. No entity is found microscopically to account for the irregularity observed grossly in one area.

d. Adrenal Glands: (Blocks - 4; sections - 4) Microscopically the adrenal glands are similar; no lesions are found to account for differences noted on gross examination. No significant alterations are found in pericapsular adipose tissue, the dense collagenous capsule, fibrous trabeculae branching from the capsule into the cortex, or in arteries, veins and nerves extending through these structures. Inflammatory cells are rarely seen; a few lymphocytes, plasma cells and monocytes infiltrate occasional perivascular regions.

Cells of zona glomerulosa form the usual oval groups or small irregular nests. These cells vary considerably in size, intensity of nuclear staining, and amount of cytoplasmic lipid; some cells contain minute yellow-brown cytoplasmic pigment granules. In most regions this zone is narrower than usual; in some places cells of zona fasciculata extend to the capsule.

Width and arrangement of cords or strands of cells in zona fasciculata are normal; there is a definite decrease in lipid content, although many individual cells have the usual vacuolated cytoplasm. Clear-cut and widespread "tubular degeneration" (Rich) is not found, but in many focal regions there are changes suggestive of early stages of this process. Capillaries extending through the zone have intact delicate walls and show no abnormalities; phagocytized material is not found in lining cells.

The zona reticularis has normal arrangement and cellularity. Abnormalities are not detected in cells containing characteristic yellow-brown pigment granules. Capillary sinusoids in superficial zones are wider than usual.

There is no sharp line of demarcation between cortex and medulla, and many nests of cortical cells are completely surrounded by medullary cells. Chromaffin and sympathetic ganglion cells and a few lymphocytes have the usual arrangement and staining qualities. Delicate supporting stroma and thin-walled capillary sinuses extend normally among nests and cords of medullary cells.

7. Central Nervous System

a. General: (Blocks - 32; sections - 32) (Figures 57-62) Significant lesions involve central nervous system diffusely; it is not necessary to describe changes separately for cerebrum, cerebellum, mid-brain, and brain stem.

b. Meninges: The outer layer of dura mater forms a normal cranial periosteum; its deeper loose connective tissue portion encloses the usual plexuses of arteries, veins and nerves. Perivascular areas are infiltrated by a few lymphocytes. The inner dural layer of dense, relatively acellular, collagenous tissue is covered by a regular layer of flattened cells. Superior sagittal sinus endothelium is intact; patent lumen contains masses of erythrocytes surrounding a small, recent fibrinous clot. Most of the numerous venous lacunae and sinuses in the vicinity of the superior sagittal sinus have thin delicate walls and contain intact erythrocytes. Extravasated erythrocytes are

seen in the loose connective tissue of the mid-dura. Some of these changes may be due to postmortem tearing of vessel walls, but existence of antemortem hemorrhage is indicated by various stages of degeneration of erythrocytes spread diffusely through stromal fibers and by inflammatory responses, including phagocytosis of cell debris and pigment. Several thin-walled sinuses are penetrated by normal arachnoid villi; some are partially calcified.

Changes in pia mater and arachnoid are not severe but are diffuse and involve almost all regions of the brain. Arachnoid trabeculations and surface layers of pia and arachnoid in several places are slightly thickened, distorted or separated by edema, infiltration by scattered inflammatory cells or focal hemorrhages. No leptomeningeal abscesses are found.

c. Blood Vessels: All parts of the brain are congested; vascular stasis is most apparent in large veins on the brain surface, but smaller veins and capillaries within brain substance are also dilated and engorged with erythrocytes. Individual erythrocyte boundaries cannot be identified in masses filling some capillaries; the lumina appear plugged by a homogeneous acidophilic gel. Most superficial veins have thin delicate walls of intact endothelium and contain well-preserved erythrocytes. Recent fibrinous clots lie among erythrocytes in a few vessels, but attachments to endothelium are not demonstrated. Small vessels on surfaces of frontal and temporal lobes contain a loose network of fibrin strands enmeshing scattered leucocytes and a few erythrocytes; the structure suggests terminal or postmortem formation. There are focal extravasations of erythrocytes into the pia-arachnoid over several areas of parietal, occipital and temporal lobes; most extravascular red blood cells are intact. The appearance suggests terminal hemorrhages with diffusion of cells accentuated by the trauma of postmortem examination. Virchow-Robin and pericapillary spaces are widened throughout the brain. Most of these spaces appear as prominent clear zones containing no stainable material; well-preserved erythrocytes, arachnoidal fibers, fibrin strands, or small clumps of proteinaceous material partially fill many perivascular zones. Generally, the process appears to be one of edema, stasis and diapedesis of red blood cells, but distinct hemorrhages beyond perivascular spaces into adjacent brain substance are present at occasional sites. These hemorrhages are all focal, and usually consist of a few well-preserved erythrocytes in loose glial tissue immediately peripheral to Virchow-Robin spaces. Most vascular alterations are in structures in the vicinity of the third ventricle, the anterior pole of the frontal lobe, the thalamus and the medulla oblongata at the level of olive.

Included in several sections are segments of major branches of cerebral and cerebellar arteries, anterior spinal, vertebral and basilar arteries. Most of these larger vessels exhibit slight sclerosis with irregular intimal widening and rare small deposits of calcium salts. Two foci of calcification in a vertebral artery have broad bases on the intact elastic lamina and extend almost completely through the thickened intima. Prominent deposits of calcium and probably other mineral salts are present in multiple small arteries within globus pallidus and immediately adjacent regions. This material is not doubly refractile. The appearance of the least involved vessels is reminiscent of a special stain for elastic lamina, since the blue-black deposits follow the contour of elastica about the entire circumference of the artery. Vessels with more advanced changes have deposits of mineral salts about collagenous and

elastic fibers, but there is little or no thickening of walls throughout all layers. Since pseudocalcification of blood vessels is often seen in these areas in normal brains, no special significance is attached to these changes. No arteries with thrombi or invasion by acute inflammatory cells are found in any part of the central nervous system.

d. Pineal Body: Normal architecture of the pineal body is severely distorted by numerous, dense, irregular, calcified masses lying in a loose reticulum of connective tissue and glial fibers. No characteristic nests of large epithelial cells remain. There are no significant inflammatory or vascular changes.

e. Ventricles; Choroid Plexuses: Most surfaces of the third, fourth and lateral ventricles are lined by the usual single layer of cuboidal or columnar epithelial cells. Short filamentous processes from free cell margins form a brush-border in some areas. Large clear cytoplasmic vacuoles beneath nuclei are most prominent in cells lining lateral ventricles. Dense, oval, eosinophilic bodies and small brown pigment granules are found in occasional cells. Ependymal surfaces are eroded in several areas and a few epithelial cells in some foci exhibit increased granularity of cytoplasm and loss of nuclei. Subependymal zones are edematous and occasionally contain scattered extravascular erythrocytes among the loose, widely separated, lightly stained glial fibers. Infiltrating cells and glial proliferation are rare. Masses of erythrocytes at several points along walls of ventricles are probably due to entry of blood during postmortem examination.

Formation of choroid plexuses is normal in all ventricles. Most of the capillary tufts contain intact erythrocytes and are covered by a normal single layer of epithelial cells. The degree of connective tissue increase and focal calcification in pericapillary regions is usual for an individual of this age.

f. Inflammatory and Degenerative Changes: No abscesses or other advanced inflammatory or degenerative lesions are found. Abnormalities in all parts of the brain are fundamentally similar and appear to be of recent development. In most instances changes can be related to the inadequacy of blood supply.

Brain substance in perivascular, subependymal and subpial regions displays varying degrees of edema, decreased affinity for stains, loss of myelin, loosening of glial fibers, and infiltration by small numbers of erythrocytes and inflammatory cells similar to those described in the meninges. Scattered inflammatory cells are most numerous in perivascular regions; dense aggregates of inflammatory cells are not seen. Large macrophages contain debris, vacuoles, or dense golden-brown pigment. Many neutrophils, monocytes and lymphocytes lie in lumina of patent capillaries along endothelial surfaces. Basophilic, non-cellular round bodies of varied sizes are often seen in these regions; some have characteristics of concretions seen in older individuals; most are fixation artifacts. Early degenerative changes are present in large nerve cells of many areas. Neurons of hippocampus, thalamic nuclei, deeper layers of cerebral cortex, and Purkinje cells of the cerebellum appear most vulnerable. Scattered cells showing varied degrees of ischemic change lie among more numerous neurons with normal morphologic characteristics. Most affected cells

are swollen and rounded, have eccentric nuclei, and are more lightly stained than usual. Normal cytoplasmic architecture is distorted by clumping or loss of Nissl substance, increased and irregular granularity, and vacuolation. Light yellow or golden-brown pigment in large neurons of many brain areas is considered within normal limits for a person of this age, but cells undergoing degenerative changes often exhibit definite chromatolysis. Lesions have not advanced sufficiently to permit development of neuronophagia or satellitosis.

Abnormalities are not found in location, structural arrangement, symmetry or types of cellular components of the various anatomically or functionally distinct parts of the brain and their interconnecting nerve pathways.

8. Musculoskeletal System

Skeletal muscle is included in sections of tongue, larynx, sternum, rib, vertebrae, esophagus, testis (cremasteric) and psoas muscle. In all regions skeletal muscle fibers are intact, have distinct cross-striations, display normal sarcolemmic nuclei, and stain lightly (probably artifactitious). No parasites are found in any fibers. Supporting connective tissue stroma extending among muscle bundles and along fascial planes is generally loose and infiltrated by scattered lymphocytes, plasma cells, monocytes and a few histiocytes, particularly in perivascular areas. No focal abscesses are found in any portion of skeletal muscle; neutrophils are rare among relatively small numbers of infiltrating cells.

In the four sections described in III. D. 4. Bone Marrow no abnormalities are found in cortical bone, cartilages of rib, sternum or vertebrae, periosteum, nor in bone structure. There is no evidence that these tissues are involved in any significant way in the inflammatory processes found in various other tissues.

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FIGURE NO. 11

SLIDE NO. 71

STAIN: H&E

MAGNIF.: X35

AFIP Neg. No. 58-14789

ORGAN; TISSUE SITE: Larynx; base of epiglottis.

REMARKS: Mucosal and submucosal edema; moderate inflammatory cell infiltrate; stasis; intact ciliated epithelium.

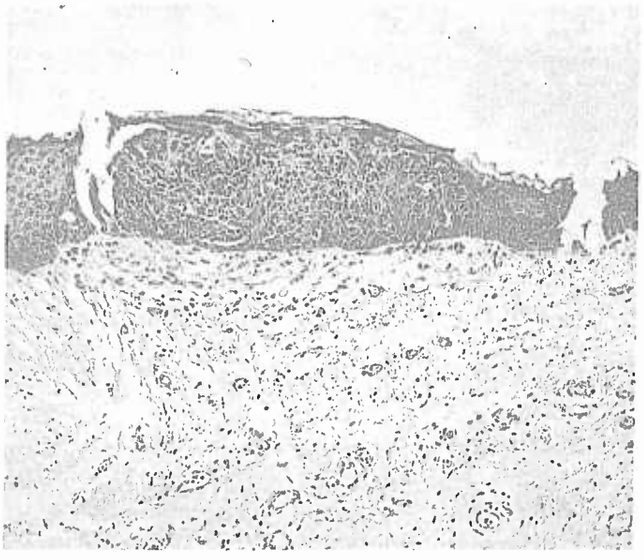

FIGURE NO. 12

SLIDE NO. 72

STAIN: H&E

MAGNIF.: X115

AFIP Neg. No. 58-14787

ORGAN; TISSUE SITE: Larnyx; vocal cord, right.

REMARKS: Focal epithelial hyperplasia; dyplasia; slight mucosal edema.

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FIGURE NO. 13

SLIDE NO. 72

STAIN: H&E

MAGNIF.: X80

AFIP Neg. No. 58-14788

ORGAN; TISSUE SITE: Larynx; immediately inferior to right vocal cord.

REMARKS: Mucosal edema; stasis, infiltration of inflammatory cells; aggregate of lymphocytes; intact ciliated epithelium.

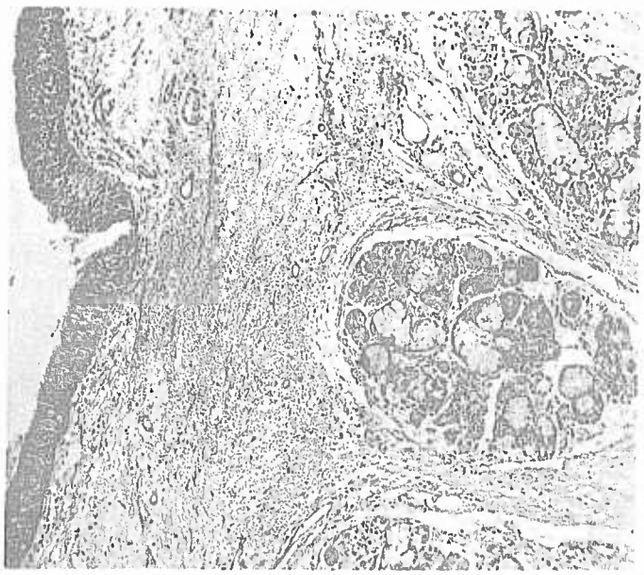

FIGURE NO. 14

SLIDE NO. 74

STAIN: H&E

MAGNIF.: X80

AFIP Neg. No. 58-14786

ORGAN; TISSUE SITE: Tracheo-laryngeal junction.

REMARKS: Mucosal stasis and hemorrhage; infiltration of inflammatory cells; relatively normal glands.

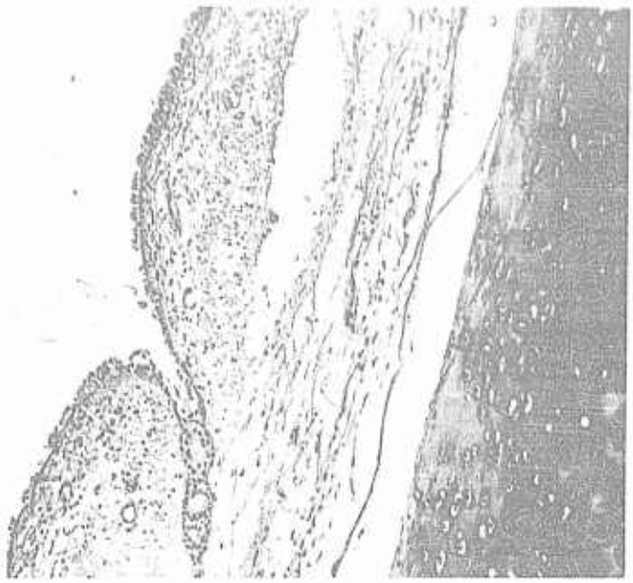

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FIGURE NO. 15

SLIDE NO. 84

STAIN: H&E

MAGNIF.: X90

AFIP Neg. No. 58-14768

ORGAN; TISSUE SITE: Trachea; 3 cm superior to bifurcation.

REMARKS: Mucosal ulceration; stasis, edema, hemorrhage; infiltration of inflammatory cells.

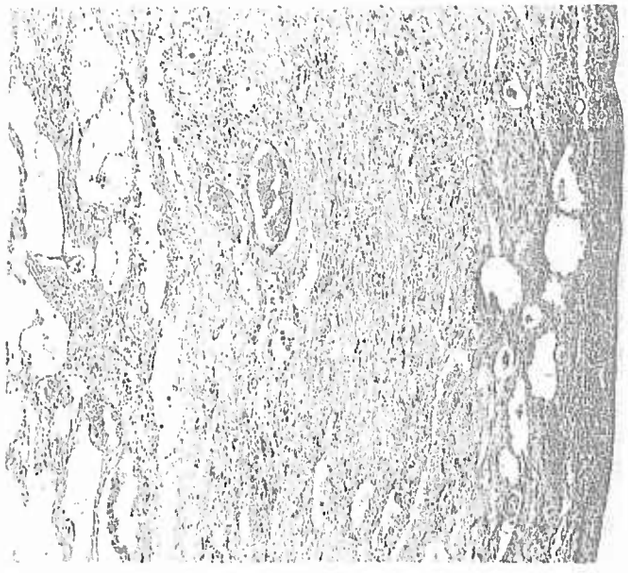


FIGURE NO. 16

SLIDE NO. 83

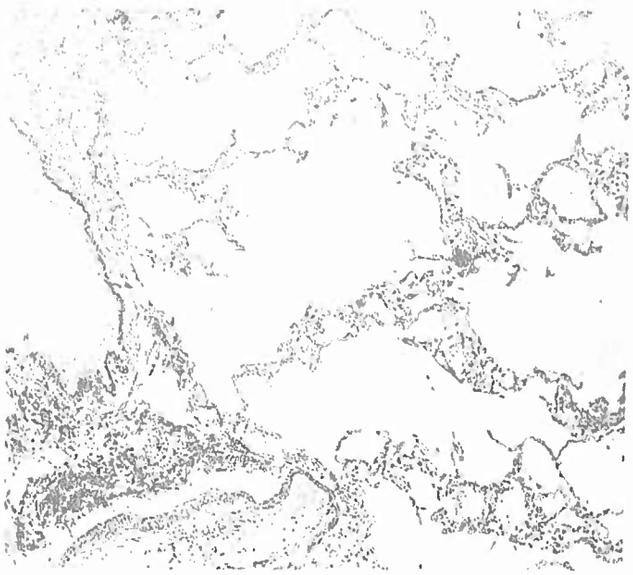
STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14785

ORGAN; TISSUE SITE: Lung; right apex.

REMARKS: Fibrosis, focal calcification (old primary tuberculous complex).



WILLARD, Joel E.
USAMU Pathology Accession No. [illegible]
5 July 1968

FIGURE NO. 17

SLIDE NO. 128

STAIN: H&E

MAGNIF.: X35

AFIP Neg. No. 58-14784

ORGAN; TISSUE SITE: Lung; 5 cm posterolateral to right apex.

REMARKS: Minimal inflammatory change; emphysema; peribronchial and perivascular anthracotic pigment.

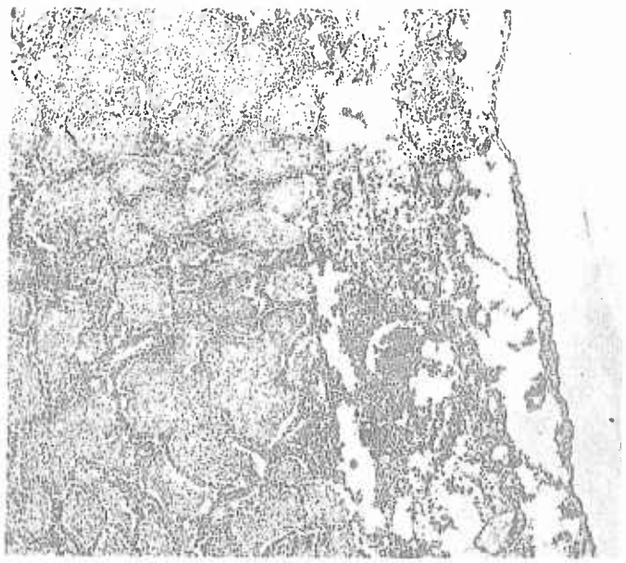


FIGURE NO. 18

SLIDE NO. 85

STAIN: H&E

MAGNIF.: X50

AFIP Neg No. 58-14783

ORGAN; TISSUE SITE: Lung; focal nodular hemorrhagic lesion, antero-inferior margin, right middle lobe.

REMARKS: Anterior margin of focal lesion; edematous subpleural zone; relatively uninvolved pleura.

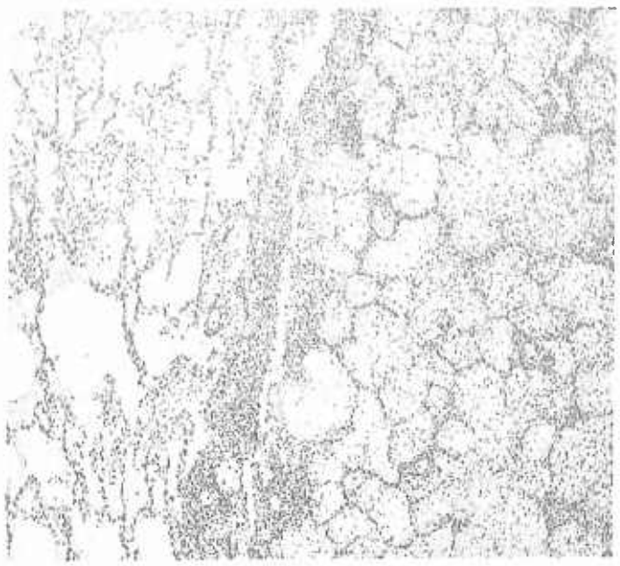


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FIGURE NO. 19

SLIDE NO. 85

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14782

ORGAN; TISSUE SITE: Lung; focal nodular hemorrhagic lesion, antero-inferior margin, right middle lobe.

REMARKS: Deep (posterosuperior margin of focal lesion; adjacent zone of alveoli filled with edema fluid.

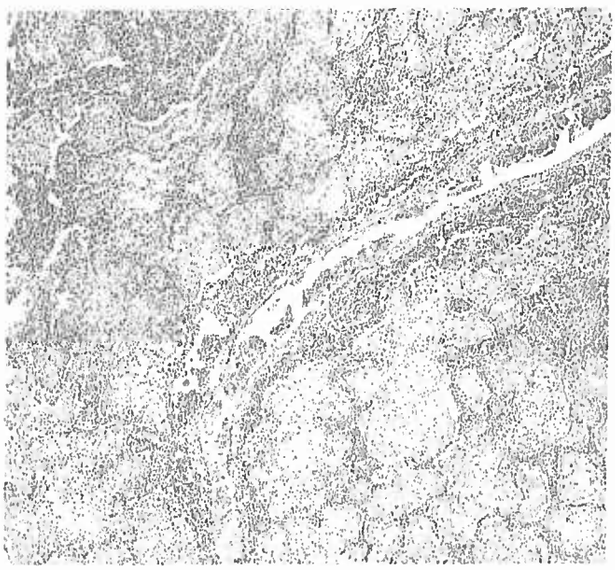

FIGURE NO. 20

SLIDE NO. 85

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14780

ORGAN; TISSUE SITE: Lung; focal nodular hemorrhagic lesion, antero-inferior margin, right middle lobe; toward center of lesion from region shown in Figure 19 above.

REMARKS: Intact red blood cells in patent artery, outer zone of focal lesion; alveoli contain fibrin plugs with scattered leucocytes; foci of early necrosis; alveolar walls are generally distinct.

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FIGURE NO. 21

SLIDE NO. 85

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14781

ORGAN; TISSUE SITE: Lung; focal nodular hemorrhagic lesion, antero-inferior margin, right middle lobe; central region.

REMARKS: Hemorrhage and necrosis; bronchus plugged with fibrinopurulent exudate; alveolar boundaries are barely discernible or lost.

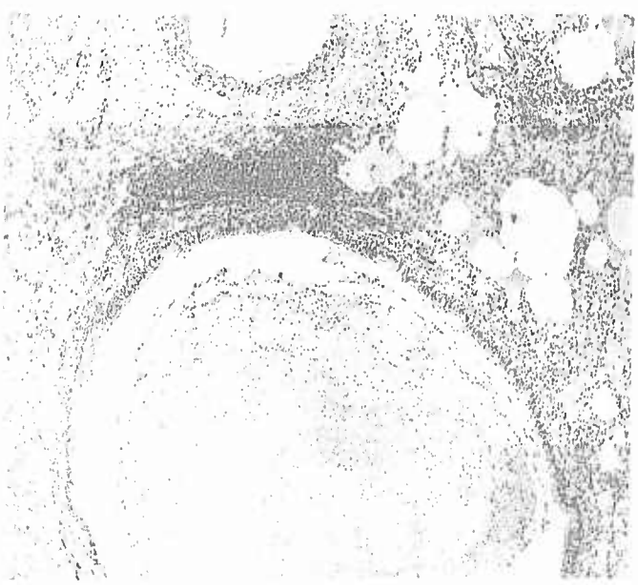

FIGURE NO. 22

SLIDE NO. 86

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14778

ORGAN; TISSUE SITE: Lung; focal nodular hemorrhagic lesion, antero-inferior margin, right middle lobe; lateral margin.

REMARKS: Bronchus with intact ciliated epithelium, plugged with fibrinous exudate containing relatively few leucocytes; peribronchial aggregate of lymphocytes; focal atelectasis, emphysema, edema.

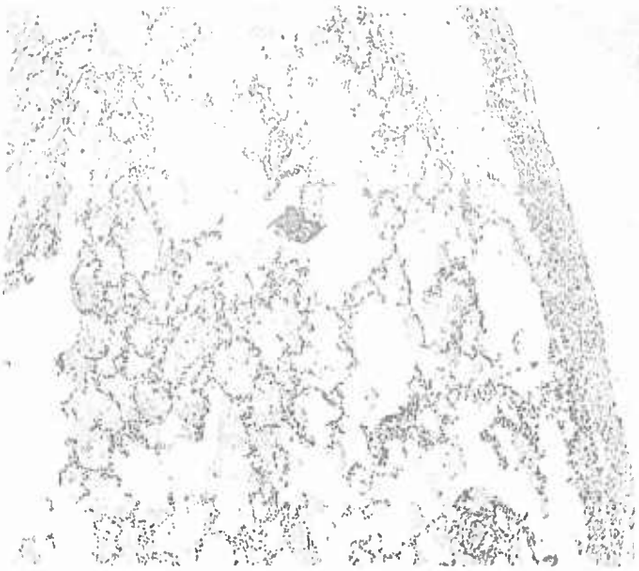

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FIGURE NO. 23

SLIDE NO. 86

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14779

ORGAN; TISSUE SITE: Lung, region immediately anterolateral to that shown in Figure 22; includes overlying pleura.

REMARKS: Relatively smooth pleura; subpleural zone of pulmonary edema, focal emphysema; minimal inflammatory changes.

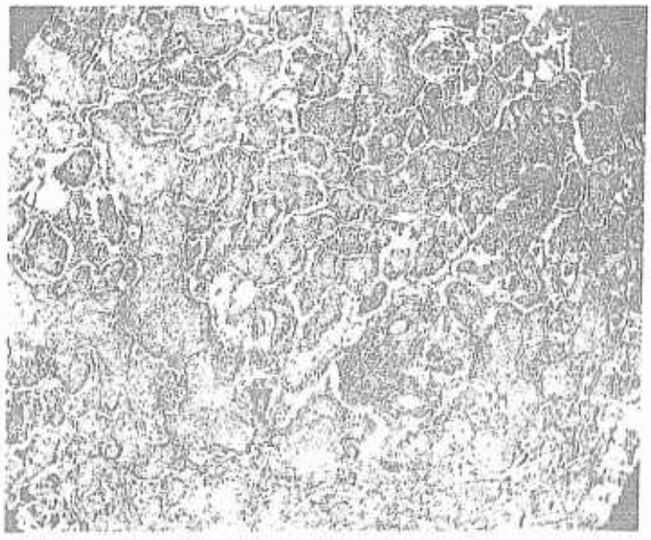

FIGURE NO. 24

SLIDE NO. 145

STAIN: Masson

MAGNIF.: X35

AFIP Neg. No. 58-14931

ORGAN; TISSUE SITE: Lung; right middle lobe, region immediately superior and medial to focal hemorrhagic lesion.

REMARKS: Alveoli filled with fibrin plugs and erythrocytes which are generally intact; most alveolar walls are intact.

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FIGURE NO. 25

SLIDE NO. 146

STAIN: Masson

MAGNIF.: X35

AFIP Neg. No. 58-14932

ORGAN; TISSUE SITE: Lung; right middle lobe, region immediately toward hilum from that shown in Figure 24; wall of large bronchus. bronchus.

REMARKS: Mucosal edema, congestion, and infiltration of lymphocytes, monocytes, plasma cells, histiocytes; intact ciliated epithelium.

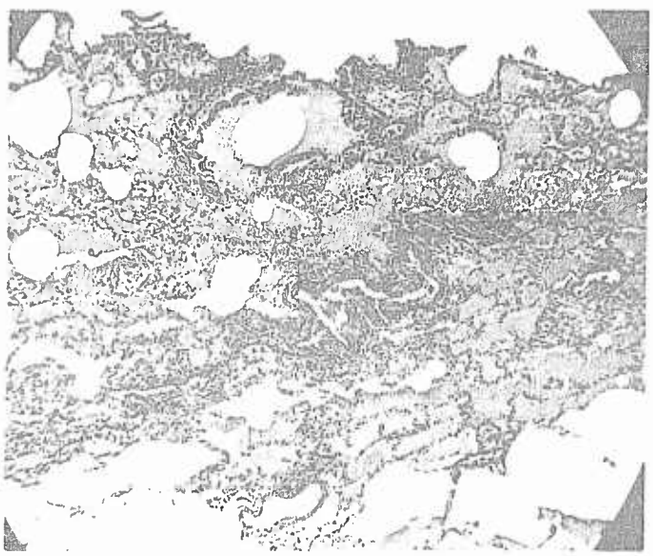

FIGURE NO. 26

SLIDE NO. 146

STAIN: Masson

MAGNIF.: X35

AFIP Neg. No. 58-14935

ORGAN; TISSUE SITE: Lung; right middle lobe, toward hilum from focal hemorrhagic region.

REMARKS: Thick-walled small vessels with perivascular pigment deposits; pulmonary edema.

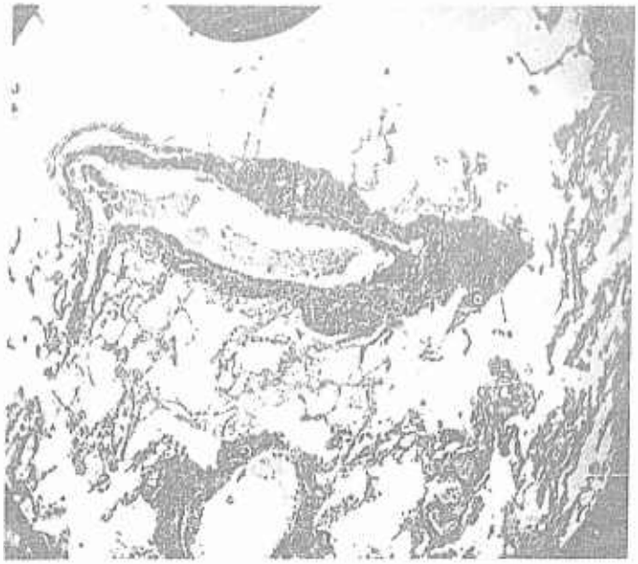

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FIGURE NO. 27

SLIDE NO. 147

STAIN: Masson

MAGNIF.: X35

AFIP Neg. No. 58-14933

ORGAN; TISSUE SITE: Lung; right middle lobe; 2 cm superior and medial to focal hemorrhagic lesion.

REMARKS: Thick-walled small vessel; dense perivascular anthracotic pigment deposits.

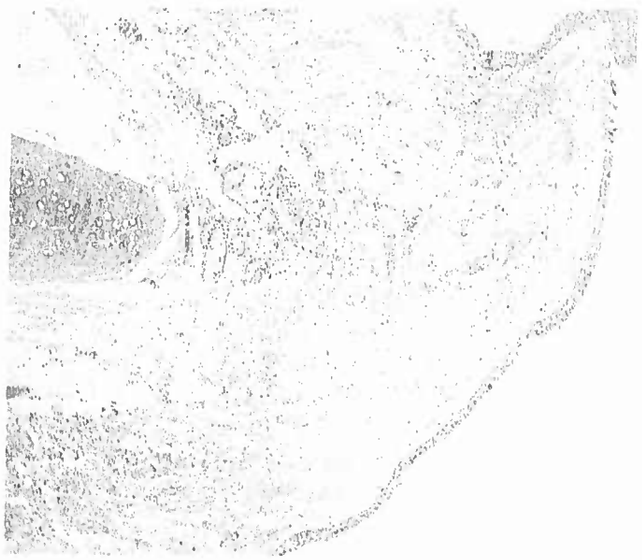

FIGURE NO. 28

SLIDE NO. 142

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14791

ORGAN; TISSUE SITE: Bronchus to right middle lobe; adjacent to lymph node in Figure 27 above.

REMARKS: Mucosal hemorrhage, edema, and inflammatory cell infiltrate; intact ciliated epithelium.

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FIGURE NO. 29

SLIDE NO. 129

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14777

ORGAN; TISSUE SITE: Lung; right lower lobe, anterior margin, lateral basal segment.

REMARKS: Focal atelectasis; thickened small arteries; perivascular fibrosis and pigment deposition; intact bronchial epithelium; almost complete absence of inflammatory changes.

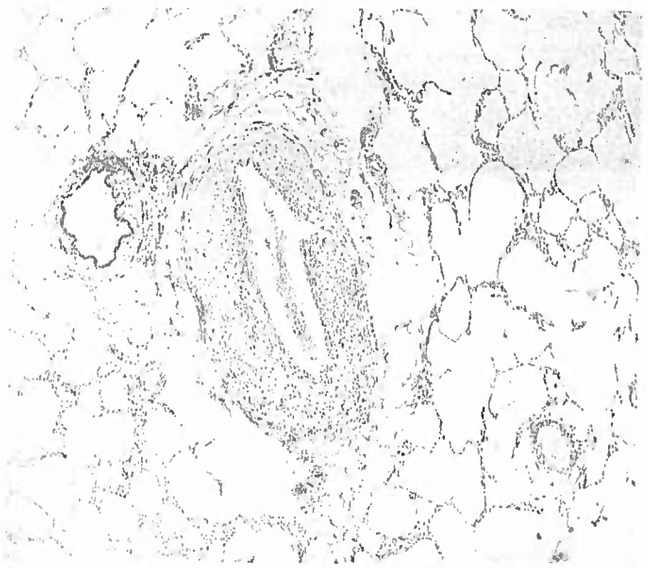

FIGURE NO. 30

SLIDE NO. 90

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14775

ORGAN; TISSUE SITE: Lung; right lower lobe, inferior margin, anterior basal segment.

REMARKS: No acute inflammatory changes; delicate alveolar walls; thick-walled artery.

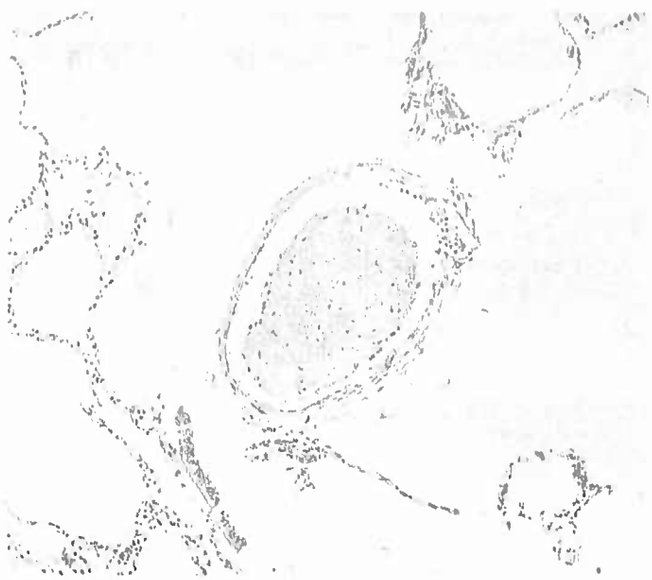

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FIGURE NO. 31

SLIDE NO. 90

STAIN: H&E

MAGNIF.: X115

AFIP Neg. No. 58-14776

ORGAN; TISSUE SITE: Lung; right lower lobe.

REMARKS: Recent thrombus, small vein; relatively normal parenchyma.

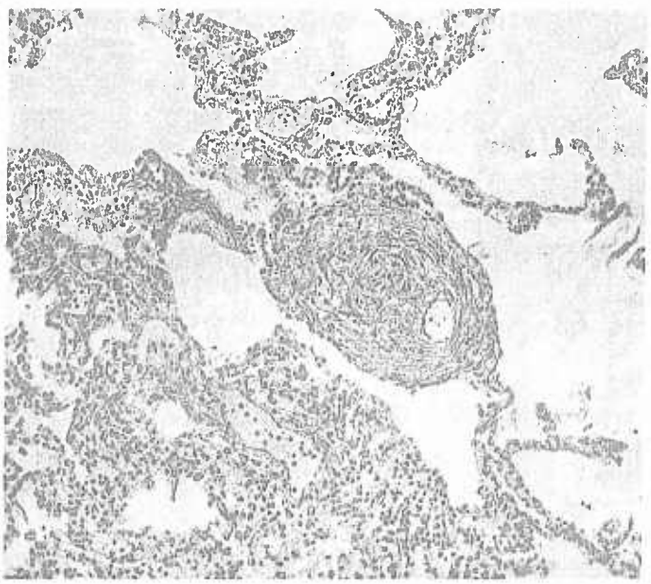

FIGURE NO. 32

SLIDE NO. 130

STAIN: H&E

MAGNIF.: X110

AFIP Neg. No. 58-14773

ORGAN; TISSUE SITE: Lung, left lower lobe, 5 cm superior to inferior margin, posterior basal segment.

REMARKS: Recanalized thrombosed artery.

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FIGURE NO. 33

SLIDE NO. 139

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14774

ORGAN; TISSUE SITE: Bronchus; to anterior segment, left upper lobe.

REMARKS: Mucosal hemorrhage, edema, and inflammatory cell infiltrate; focal erosion of epithelium.

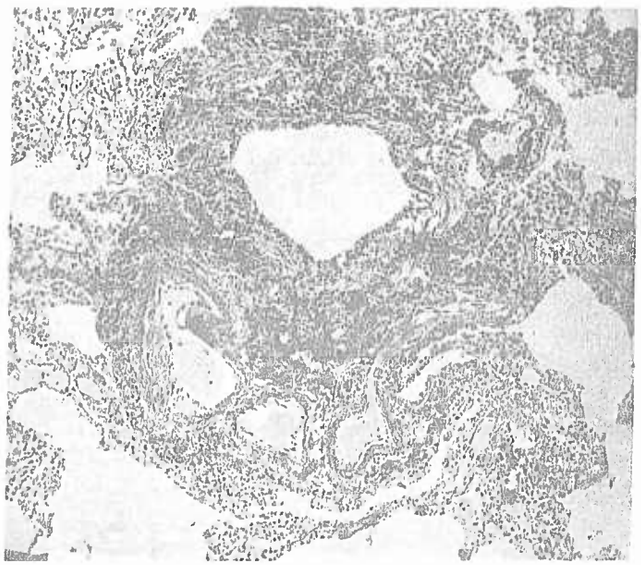

FIGURE NO. 34

SLIDE NO. 130

STAIN: H&E

MAGNIF.: X80

AFIP Neg. No. 58-14772

ORGAN; TISSUE SITE: Lung; left lower lobe.

REMARKS: Peribronchial and periarterial pigment deposition, fibrosis; thickened small arteries.

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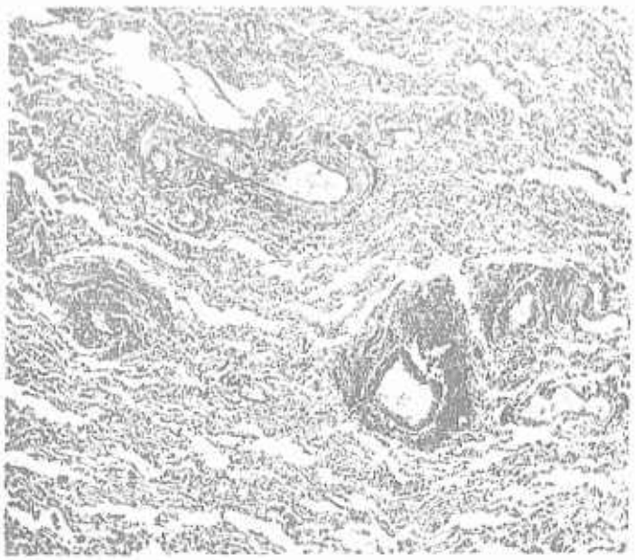

FIGURE NO. 35

SLIDE NO. 149

STAIN: Masson

MAGNIF.: X40

AFIP Neg. No. 58-14934

ORGAN; TISSUE SITE: Lung; left lower lobe, posterior basal segment.

REMARKS: Thick-walled small vessels; perivascular pigment deposits; atelectasis; almost complete absence of acute inflammation.

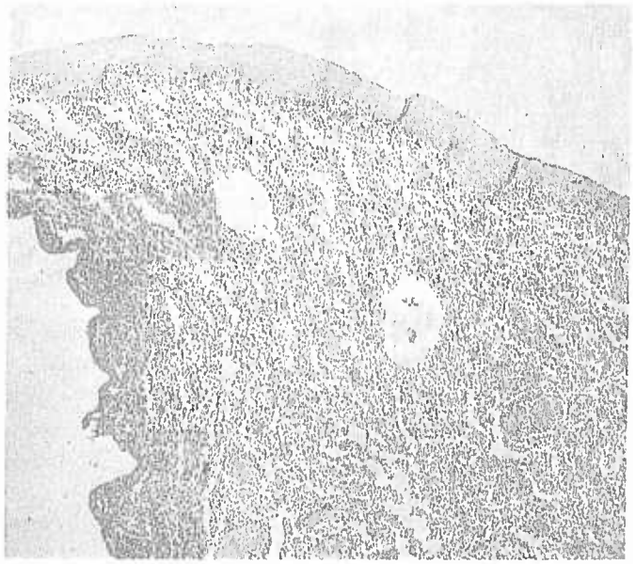

FIGURE NO. 36

SLIDE NO. 1

STAIN: H&E

MAGNIF.: X60

AFIP Neg. No. 58-14762

ORGAN; TISSUE SITE: Spleen.

REMARKS: Portion of wall of subcapsular cyst.

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FIGURE NO. 37

SLIDE NO. 69

STAIN: B&B

MAGNIF.: X625

AFIP Neg. No. 58-14794

ORGAN; TISSUE SITE: Lymph node; paratracheal, right, 1 cm inferior to thyroid.

REMARKS: Necrotic, edematous and hemorrhagic area of hyperplastic node; organisms with morphological features of B. anthracis.

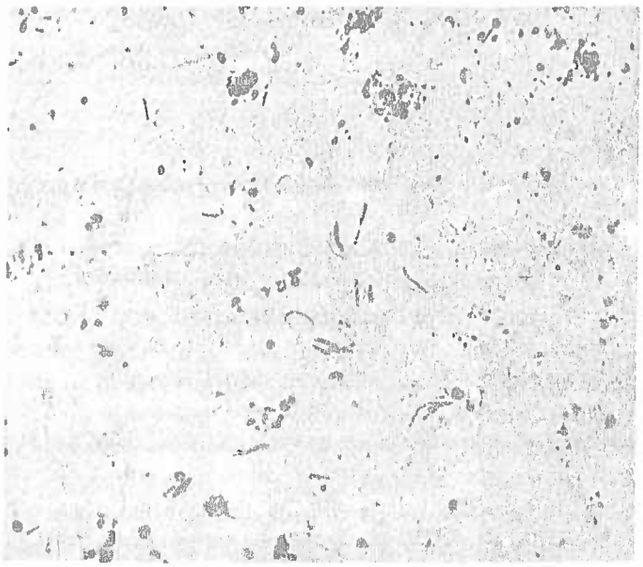

FIGURE NO. 38

SLIDE NO. 88

STAIN: B&B

MAGNIF.: X625

AFIP Neg. No. 58-14797

ORGAN; TISSUE SITE: Lymph node; antero-inferior to bifurcation of trachea.

REMARKS: Area of hemorrhage and necrosis; organisms with morphological features of B. anthracis.

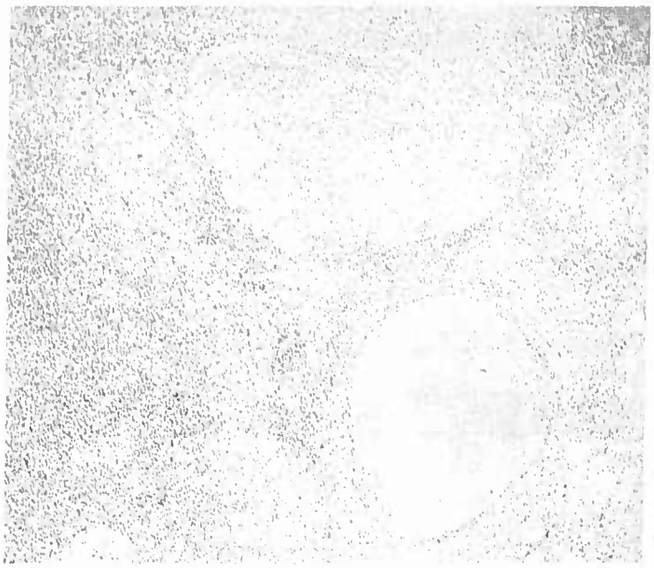

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FIGURE NO. 39

SLIDE NO. 88

STAIN: H&E

MAGNIF.: X35

AFIP Neg. No. 58-14799

ORGAN; TISSUE SITE: Lymph node; antero-inferior to bifurcation of trachea.

REMARKS: Vicinity of field shown in Figure 38; hemorrhage, edema, congestion, thrombosed vessels; acute inflammation, necrosis.

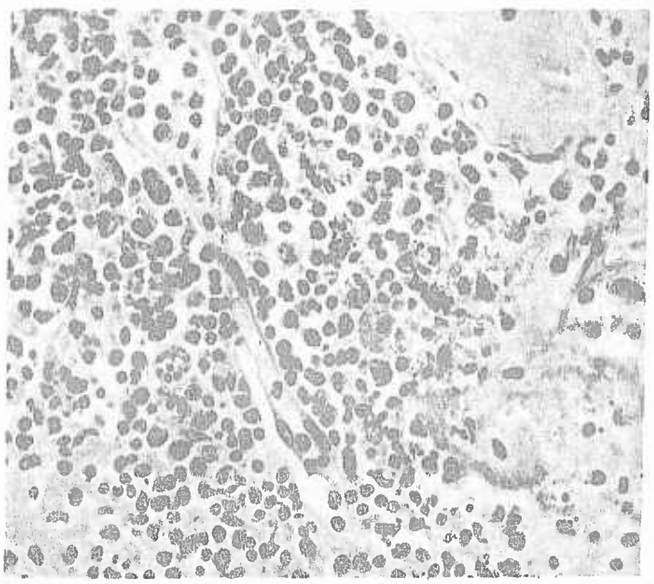

FIGURE NO. 40

SLIDE NO. 88

STAIN: H&E

MAGNIF.: X625

AFIP Neg. No. 58-14798

ORGAN; TISSUE SITE: Lymph node; antero-inferior to bifurcation of trachea.

REMARKS: High power view of area of Figure 39 above showing reactive cells, congestion, and edema.

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FIGURE NO. 41

SLIDE NO. 88

STAIN: B&B

MAGNIF.: X625

AFIP Neg. No. 58-14796

ORGAN; TISSUE SITE: Lymph node; antero-inferior to bifurcation of trachea.

REMARKS: Area of hemorrhage, necrosis, edema; organisms with morphological features of B. anthracis.

FIGURE NO. 42

SLIDE NO. 76

STAIN: B&B

MAGNIF.: X625

AFIP Neg. No. 58-14795

ORGAN; TISSUE SITE: Lymph node; paratracheal, anterolateral to trachea, 3 cm above bifurcation.

REMARKS: Area of hemorrhage, edema and necrosis; organisms with morphological features of B. anthracis.

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FIGURE NO. 43

SLIDE NO. 141

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14793

ORGAN; TISSUE SITE: Lymph node; between pulmonary artery and right main stem bronchus.

REMARKS: Hyperplasia, congestion, edema, hemorrhage into dilated peripheral sinus; extension of process through capsule into pericapsular fat.

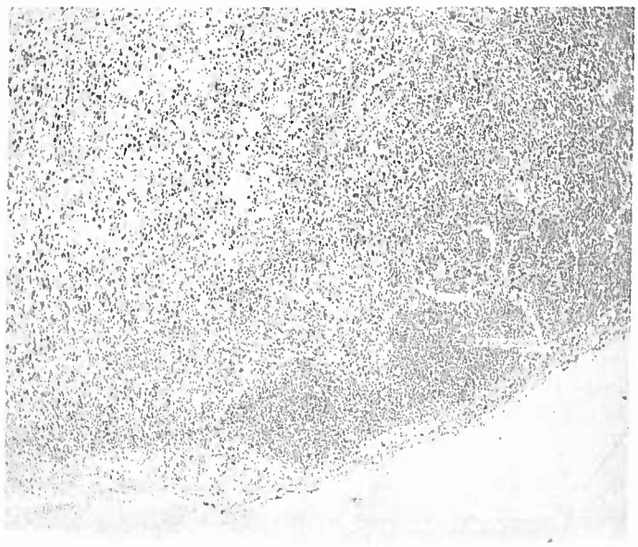

FIGURE NO. 44

SLIDE NO. 126

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14792

ORGAN; TISSUE SITE: Lymph node; inferomedial to bifurcation of left bronchus, adjacent to pulmonary vein.

REMARKS: Hyperplasia, edema, hemorrhage, examples of rare intact follicles, dilated peripheral sinus.

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FIGURE NO. 45

SLIDE NO. 142

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14790

ORGAN; TISSUE SITE: Lymph node; adjacent to bronchus to right middle lobe.

REMARKS: Focus of old calcification and fibrosis (primary tuberculosis complex?), surrounded by region of recent hemorrhage, necrosis, hyperplasia, and edema.

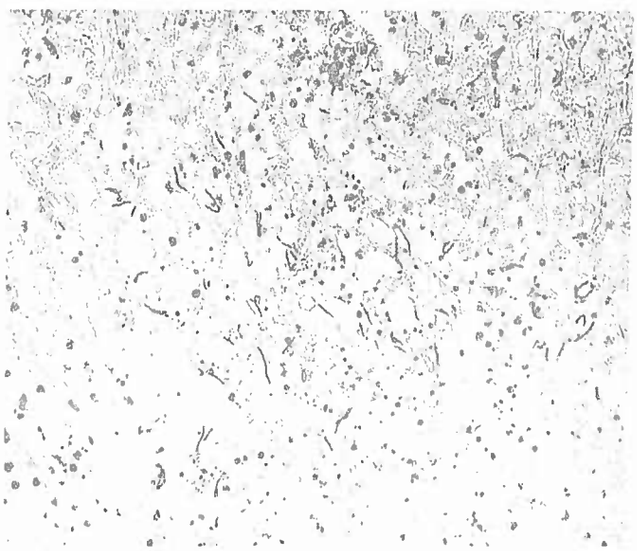

FIGURE NO. 46

SLIDE NO. 77

STAIN: B&B

MAGNIF.: X305

AFIP Neg. No. 58-14929

ORGAN; TISSUE SITE: Lymph node; paratracheal, right, 3 cm above bifurcation of trachea.

REMARKS: Numerous bacilli with morphological features of B. anthracis are scattered through necrotic hemorrhagic focus.

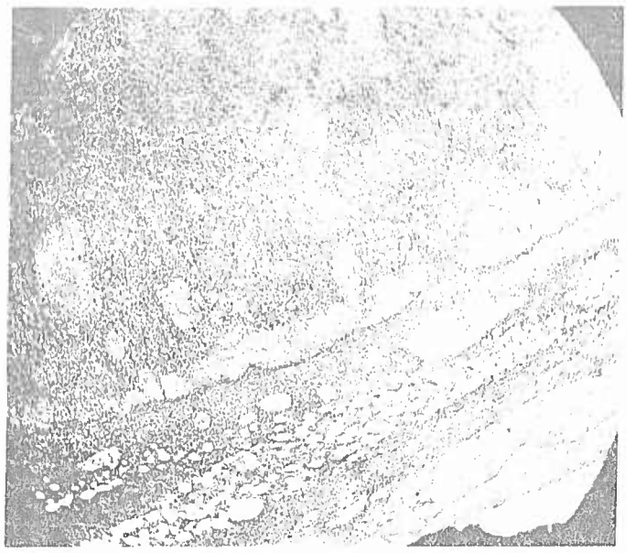

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FIGURE NO. 47

SLIDE NO. 88

STAIN: Retic.

MAGNIF.: X35

AFIP Neg. No. 58-14928

ORGAN; TISSUE SITE: Lymph node; antero-inferior to bifurcation of trachea.

REMARKS: Widened sinuses contain loose reticulum of fibrin strands which enmesh monocytes and large macrophages; edema; congestion; hyperplasia; extension of inflammatory process through capsule into adjacent mediastinal adipose and connective tissues.

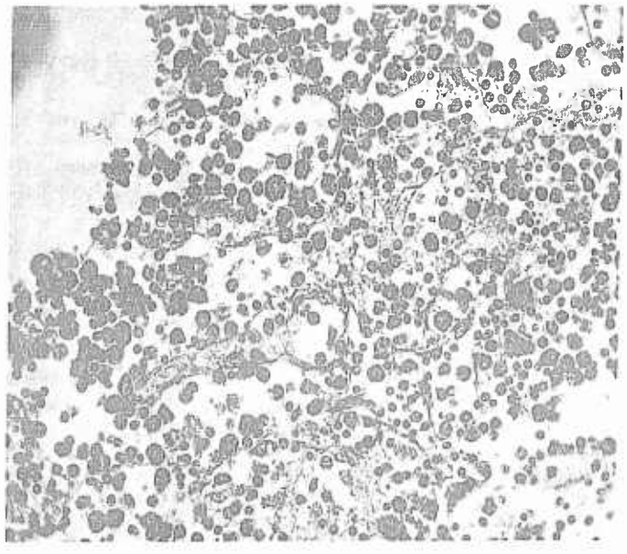

FIGURE NO. 48

SLIDE NO. 142

STAIN: Giemsa

MAGNIF.: X305

AFIP Neg. No. 58-14930

ORGAN; TISSUE SITE: Lymph node; anterior to bifurcation of right main stem bronchus.

REMARKS: Widened subcapsular sinuses; reticulum cell hyperplasia; large histiocytes, pleomorphic phagocytic cells, vacuolated monocytes, plasma cells and lymphocytes.

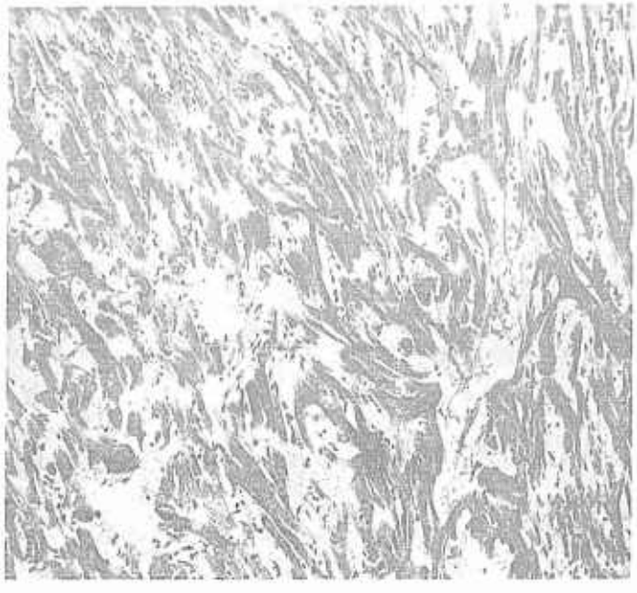

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FIGURE NO. 49

SLIDE NO. 93

STAIN: H&E

MAGNIF.: X100

AFIP Neg. No. 58-14771

ORGAN; TISSUE SITE: Heart; left ventricle, 6 cm superior to apex.

REMARKS: Myocardial edema; fragmented muscle fibers.

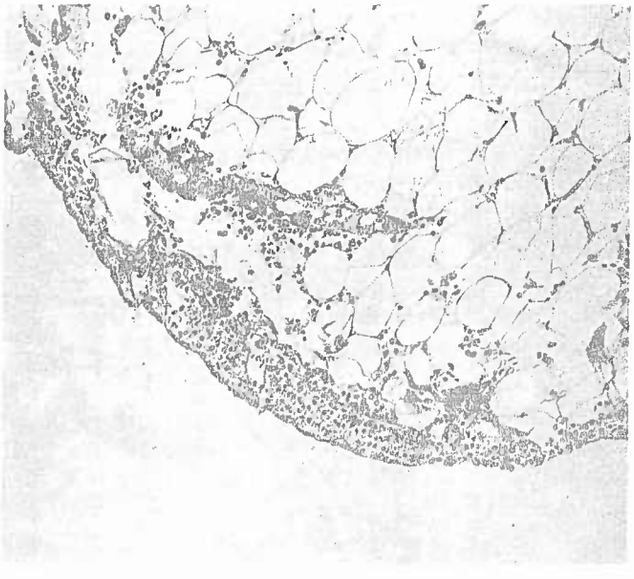

FIGURE NO. 50

SLIDE NO. 93

STAIN: H&E

MAGNIF.: X120

AFIP Neg. No. 58-14770

ORGAN; TISSUE SITE: Heart; left ventricle, near apex.

REMARKS: Congestion and infiltration of inflammatory cells, epicardium.

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FIGURE NO. 51

SLIDE NO. 62

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14767

ORGAN; TISSUE SITE: Esophagus; upper third.

REMARKS: Mucosal congestion, edema, infiltration of inflammatory cells; focal ulceration.

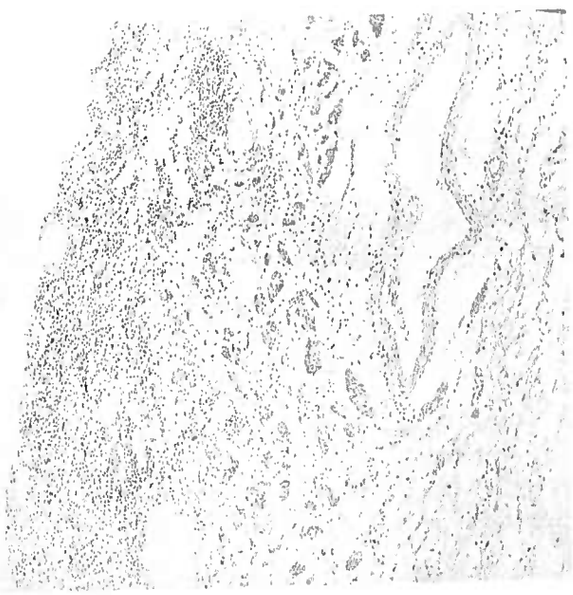

FIGURE NO. 52

SLIDE NO. 89

STAIN: H&E

MAGNIF.: X60

AFIP Neg. No. 58-14766

ORGAN; TISSUE SITE: Esophagus; at level of tracheal bifurcation.

REMARKS: Complete ulceration of mucosal epithelium; mucosal and submucosal edema, congestion, focal hemorrhages, infiltration of monocytes, lymphocytes, plasma cells and few granulocytes.

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FIGURE NO. 53

SLIDE NO. 48

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14769

ORGAN; TISSUE SITE: Jejunum; focal lesion involving entire wall.

REMARKS: Necrosis with almost complete loss of cell detail throughout mucosa and submucosa; edema, congestion and severe acute inflammatory reaction of outer layers.

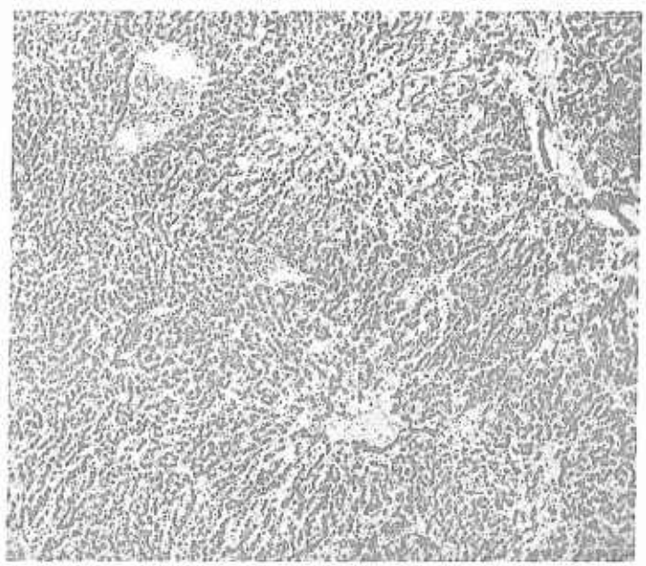

FIGURE NO. 54

SLIDE NO. 25

STAIN: H&E

MAGNIF.: X50

AFIP Neg. No. 58-14763

ORGAN; TISSUE SITE: Liver.

REMARKS: Congestion; lymphocytic infiltration of portal areas.

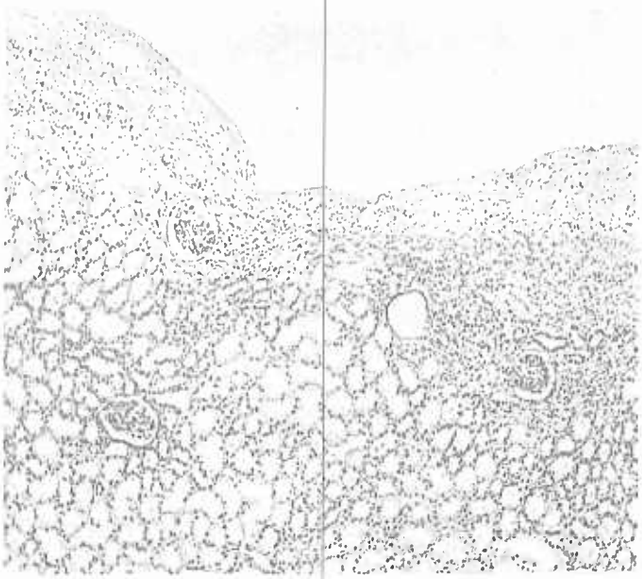

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FIGURE NO. 55

SLIDE NO. 11

STAIN: H&E

MAGNIF.: X60

AFIP Neg. No. 58-14765

ORGAN; TISSUE SITE: Kidney; right.

REMARKS: Wall of subcapsular cyst; relatively normal parenchyma deep to connective tissue of cyst wall.

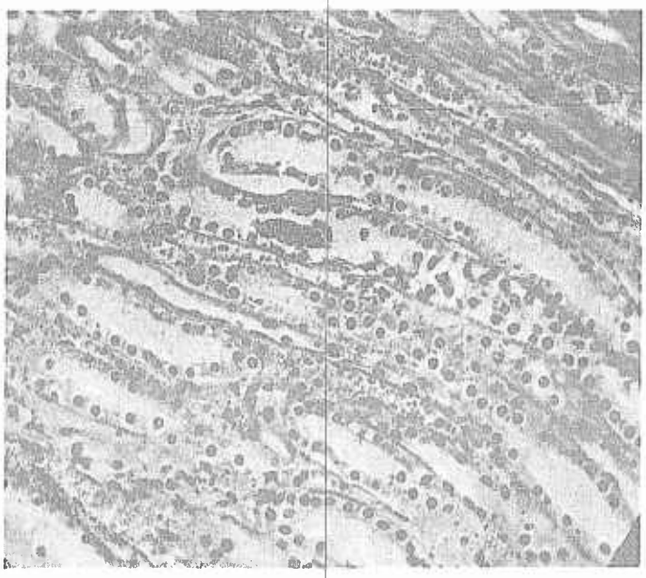

FIGURE NO. 56

SLIDE NO. 13

STAIN: H&E

MAGNIF.: X265

AFIP Neg. No. 58-14764

ORGAN; TISSUE SITE: Kidney; left.

REMARKS: Relatively normal parenchyma; hyaline cast; slight tubular epithelial degenerative changes; slight stasis; occasional epithelial cells contain golden brown pigment granules.

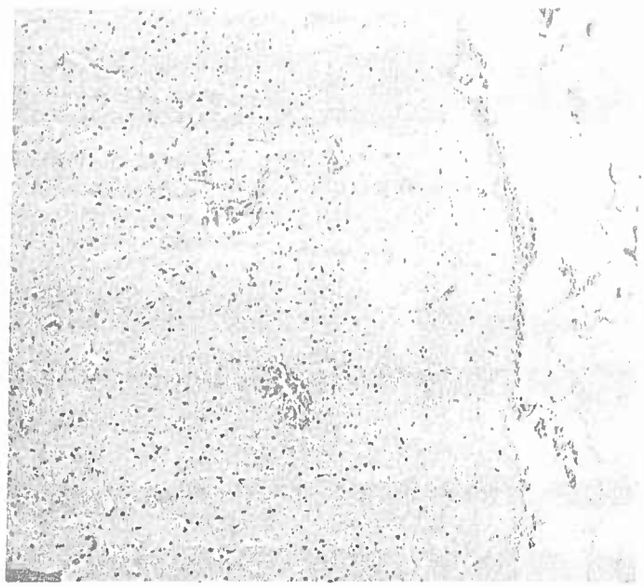

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FIGURE NO. 57

SLIDE NO. 98

STAIN: H&E

MAGNIF.: X60

AFIP Neg. No. 58-14761

ORGAN; TISSUE SITE: Brain; superior surface, left frontal lobe.

REMARKS: Stasis; pia-arachnoid and perivascular focal hemorrhage.

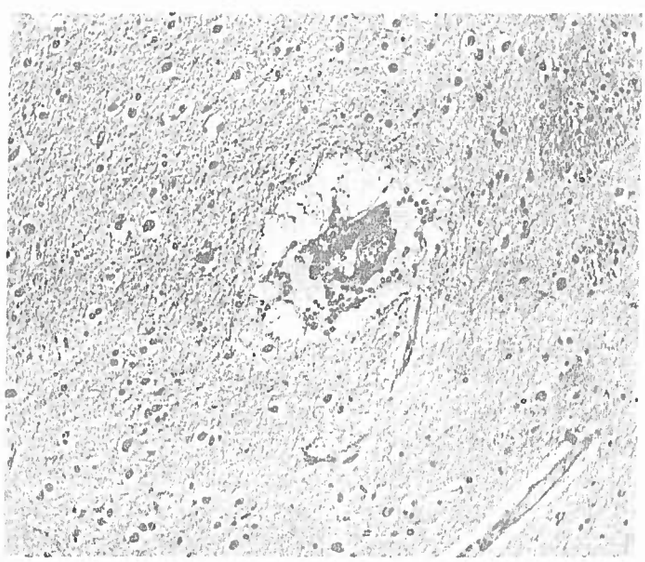

FIGURE NO. 58

SLIDE NO. 107

STAIN: H&E

MAGNIF.: X145

AFIP Neg. No. 58-14927

ORGAN; TISSUE SITE: Brain; small vessel near left wall of lateral ventricle, superior to region of optic chiasm.

REMARKS: Dilated vein; perivascular edema; infiltration of few lymphocytes and monocytes; early degenerative changes of parenchyma immediately about vessel.

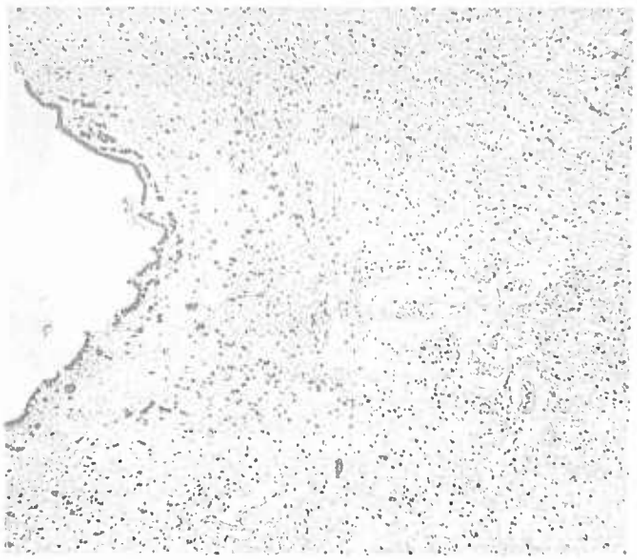

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FIGURE NO. 59

SLIDE NO. 110

STAIN: H&E

MAGNIF.: X90

AFIP Neg. No. 58-14926

ORGAN; TISSUE SITE: Brain; region of caudate nuclei; wall of lateral ventricle and subependymal small thick-walled vessels.

REMARKS: Walls are composed mainly of a zone of non-cellular, lightly stained, acidophilic hyaline material.

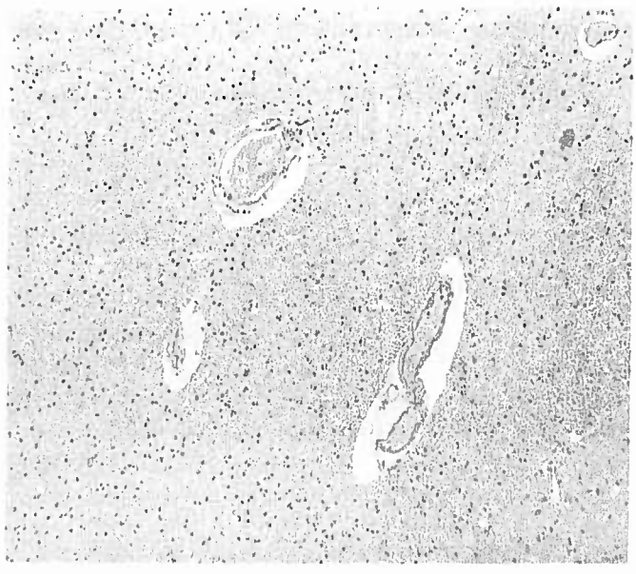

FIGURE NO. 60

SLIDE NO. 111

STAIN: H&E

MAGNIF.: X90

AFIP Neg. No. 58-14925

ORGAN; TISSUE SITE: Brain; region of external capsule and putamen.

REMARKS: Small vein with recent thrombus or embolus; paucity of inflammatory cells; perivascular edema.

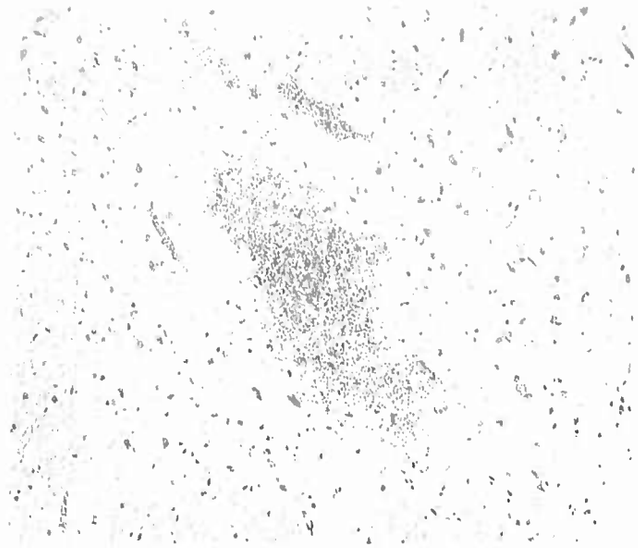

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FIGURE NO. 61

SLIDE NO. 117

STAIN: H&E

MAGNIF.: X85

AFIP Neg. No. 58-14923

ORGAN; TISSUE SITE: Medulla oblongata; level of olive.

REMARKS: Stasis and recent perivascular hemorrhage; erythrocytes in parenchyma are generally intact.

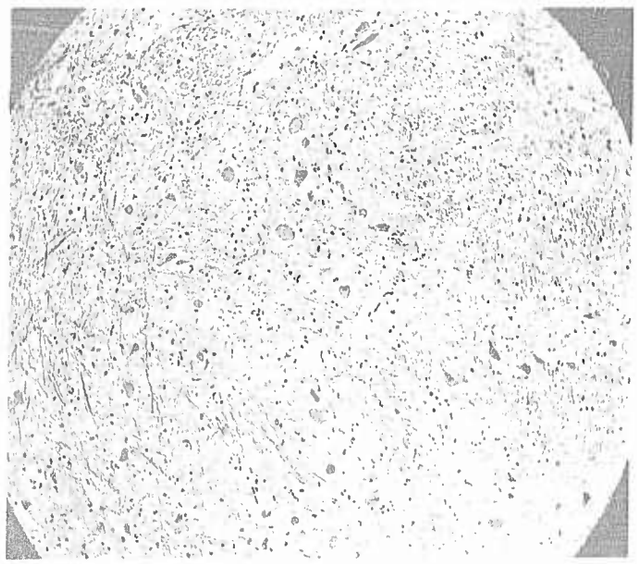

FIGURE NO. 62

SLIDE NO. 117

STAIN: H&E

MAGNIF.: X85

AFIP Neg. No. 58-14924

ORGAN; TISSUE SITE: Medulla oblongata; level of olive.

REMARKS: Early degenerative changes in neurons.

VI. DISCUSSION

The clinical diagnosis of anthrax in this 53 year old electrician was confirmed by the demonstration of B. anthracis and of characteristic tissue changes. The time and the source of his exposure are not known.

The post mortem examination disclosed a number of abnormalities which antedate the terminal illness. This case afforded an opportunity to examine the possible role of anatomical and physiological alterations as predisposing factors to the establishment of the initial infection, or which may have modified the actual course of the disease as it developed.

There were certain pre-existing abnormalities which possibly reduced the mechanical and physiological effectiveness of the upper respiratory tract as a filtering or impinging device. These were:

1. Obstruction of the nasal passages due to distortion and deviation of the nasal septum.

2. Asymmetry of the epiglottis.

3. Distortion of the laryngeal cavity due to an old dislocation and marked asymmetry of the thyroid cartilages.

4. Distortion and scarring of the right vocal cord resulting from excision of focal carcinoma.

There was also old bilateral, apical, pulmonary fibrosis and calcification of the type commonly attributed to old healed tuberculosis. Associated with this was extensive scarring and calcification in the right hilar and tracheobronchial lymph nodes. The most marked calcification was in a node of the right laterotracheal chain and it was this node that yielded the only positive cultures for B. anthracis obtained at autopsy. The exact etiology of this scarring and calcification is not apparent and probably is not relevant. The important feature was the degree of compromise of the lymphatics at the time of the exposure to anthrax.

There was considerable anthracotic pigmentation and readily visible silica throughout both lungs but the classical picture of severe fibrosis was missing. The occupational history provides a ready explanation of these findings.

It would appear that the initial anthrax lesion was in the right middle lobe. This lesion was discernible on the roentgen film 24 hours after onset of fever, and there was no evidence of a retrograde lymphatic extension as a method of development. From this area alone, traces of beryllium were demonstrated by spectrographic analysis. In a series of chest roentgenograms on this man over a period of years there was a 1952 film which showed a hazy opacity seemingly at this identical site. There was a history consistent with exposure to beryllium. All that one could do was to note the remarkable identity in the location of the single pulmonary focus of hemorrhagic inflammatory changes with the 1952 lesion, the identification of beryllium from this area, and the recovery of viable B. anthracis from the calcified lymph nodes draining this segment of lung.

Turning from these long-standing anatomical alterations to another series of events, the immunological status of this man is of considerable interest. Less than two weeks prior to the onset of his terminal illness he had received vaccinations for yellow fever (17D) and for small pox. At this time he also was given two injections of Foshay-type tularemia vaccine. Maximal response of man to yellow fever vaccine is at the 5-10 day period post-vaccination. The time of exposure to B. anthracis is not known but the commonly accepted incubation period of 5-7 days would mean an exposure to B. anthracis at the time of the maximal reaction to the 17D yellow fever virus. The circumstances require serious consideration of an "immunological pre-occupation" with a virus infection involving reticulo-endothelial cells and existing at the time of initial entry of B. anthracis into the lymphatic system.

Thus, insofar as initiation of the infection is concerned, this man had a group of pre-existing abnormalities capable of reducing the effectiveness of his upper respiratory tract as a filtering or impinging device; the presumed initial anthrax lesion developed in an area of lung from which beryllium was isolated; there was marked old calcification in the lymph nodes draining this area; and during the "incubation period" his reticulo-endothelial system was engaged in handling one or two active virus infections resulting from vaccine.

The source of the single lesion in the small bowel cannot be determined. Although the possibility of vascular dissemination must be admitted because of initial septicemia, the absence of other abdominal lesions weighs against it. Whatever may have been the genesis, this gut involvement seems an incidental finding.

Turning now to a consideration of the course of the disease, the abrupt onset of fever and other symptoms is consistent with earlier reports concerning respiratory anthrax. At 24 hours there was clear roentgen evidence of involvement in the right middle lobe and striking involvement of the mediastinal lymphoid tissues. No other specific lung lesions developed either before or during therapy, and this coupled with the histologic appearance of the right middle lobe lesion suggests that it was the primary focus, followed by mediastinal involvement, associated with, or followed by, a low level bacteremia. Lung lesions, comparable in histologic character, have been produced in experimental animals exposed to aerosolized B. anthracis spores.

The initiation of therapy 54 hours post-onset of fever did not favorably alter the progress of the disease picture, although the septicemia was controlled and there was a continuing decline of fever. It is significant that at no time during his illness did this man show any evidence of a systemic toxin effect. There was no evidence of peripheral vascular collapse, nor lowered blood pressure. His urine output remained good; histologically there was no "lower nephron" involvement. At autopsy no "toxin" could be demonstrated by a variety of methods.

It is essential to establish that the clinical picture was representative of untreated "woolsorter's disease." To find such cases in any number, reference must be made to the Bradford outbreaks of the 1880's described in detail by Greenfield[1] and Spear[2]. In their reports are case histories and autopsy findings which, without editing, could be substituted for the present case. It

is difficult to understand why current texts do not allude to these early clinical and laboratory descriptions.

Then, in both treated and untreated cases a factor held in common is the presence of involvement of the mediastinum, the classical lesion of "woolsorter's disease." These findings have been extensively considered in the foregoing protocol, but it must again be emphasized that widening of the mediastinum was an initial finding, being present 24 hours post-onset of fever and probably being due at that time to a marked hyperplasia of the mediastinal lymph nodes. The time of the hemorrhage into these nodes cannot be determined with certainty but in the subsequent 24 hours there was roentgen evidence of the appearance of pleural fluid. Therapy begun at this time apparently did not alter the further evolution of these lesions. In cutaneous anthrax treated with penicillin, Ellingson, et al[3] noted "the anthrax lesion continued to advance through a well defined and typical cycle, in spite of treatment and in spite of the absence of viable organisms." With mediastinal lesions, as with the cutaneous lesions, it would appear that if a "toxin" plays a part in the picture the role is to produce a local necrotizing effect at the area of involvement, this to be followed by hemorrhage and edema. Such an effect seems to be compatible with the findings of Smith, et al[4], on in vivo-produced toxin in the anthrax-infected guinea pig. The toxic factor was associated with large numbers of organisms, and when injected intradermally resulted in vascular damage, edema and hemorrhage.

Compromise of the lymphatic system was obvious and undoubtedly initiated and continued to provoke the increasing accumulation of pleural fluid. This probably was followed by pressure on the next most vulnerable component of the mediastinum, the venous system with resultant stasis involving the major and minor circulation. Associated with this was a decrease in respiratory exchange, each component contributing to, and being supplemented by, the other. With the progressive accumulation of pleural fluid there was an increased air hunger for which oxygen was only palliative. In the terminal hours suprasternal and facial cyanosis was apparent. The histologic picture in the brain with recent perivascular hemorrhage was entirely consistent with the state of anoxia described and which, in turn, contributed to the downward progression.

The fact that therapy initiated at 54 hours resulted in complete suppression of the septicemia but did not alter the continued progress of the infection in its classical form suggests strongly that in man, as in other species, bacteremia is not an essential component of "woolsorter's disease."

A significant point in the present case is the roentgen evidence of a focal lung lesion and of mediastinitis present in a febrile individual. The extensive mediastinal involvement initially associated with relatively bland systemic manifestations was such as to suggest a lymphoma or a metastatic malignancy. The critical question of when in the pathogenesis of this infection this lesion appeared is not answerable, but by inference from animal studies, and from the extensiveness at 24 hours post-onset of fever in man, it probably could have been observed even earlier in the course of the illness. This is the earliest x-ray examination of man on record, and, if the case is truly representative, the picture is such that respiratory anthrax should be readily recognizable at an early stage.

In the present case, once the diagnosis was established, the principal concern was with an effort to handle peripheral vascular collapse or renal failure, both of which have been described in experimental animals. Each therapeutic measure was evaluated and weighed with regard to likelihood that it would precipitate one or the other. Actually neither appeared, and while both phenomena may be seen in animals treated late or in untreated man it is obvious that they are secondary. Their absence, probably because of drug therapy, did not in any way alter the basic course of the disease, forcing one to the conclusion that the rapid development of space-occupying lesions in the mediastinum is of primary importance and implying that vigorous therapeutic countermeasures, in addition to early antibiotics, are mandatory.

These countermeasures should perhaps include early tracheotomy, repeated or continuous aspiration of the pleural cavities, careful maintenance of fluid balance, use of positive pressure respiration equipment, and finally, possible surgical relief of the mediastinal embarrassment if other measures fail. A continuous oximeter and a continuous venous pressure recording would appear paramount for following the course of physiological changes.

Recently completed studies on respiratory anthrax of monkeys and sheep show that with appropriate manipulation of drug schedules, involvement of the mediastinum, in a manner comparable to that described in this case, regularly occurs. Such animals die showing only a low level terminal bacteremia.

It thus seems clear that the mechanism of death in certain forms of anthrax is due to space-occupying lesions in the mediastinum. The entire clinical course can be explained on this basis and there is no requirement to invoke septicemia or a systemic toxic effect, nor in this case is there any evidence that either was active or important. (The possible local role of a toxin in the initiation of destruction of lymphoid tissue in the mediastinum has been mentioned earlier.) A tentative explanation is thus afforded for the critical factor of time of initiation of chemotherapy in anthrax involving the mediastinum.

REFERENCES:

1. Greenfield, W. S.: "Further investigations on anthrax and allied diseases in man and animals, Lecture III," The Lancet, I:91-94, 1881 --- Lecture IV, Ibid, 163-164, 1881.

2. Spear, J.: "On the so-called "Woolsorters' Disease" as observed at Bradford and in neighboring districts of the West Riding of Yorkshire," in Appendix A, No. 8, of the 10th Annual Report of the Local Government Board, 66-135, London, 1880-81.

3. Ellingson, H. V., Kadull, P. J., Bookwalter, H. L., and Howe, C.: "Cutaneous Anthrax, Report of twenty-five cases," J Am Med Ass, 131:1105-1108, 1946.

4. Smith, H., Keppie, J., and Stanley, J. L.: "The chemical basis of the virulence of Bacillus anthracis. V. The specific toxin produced by B. anthracis in vivo," Brit J Expt Path, 36:460-472, 1955.